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HISTONE ZINC INSULIN, GLOBIN (ZINC) INSULIN AND CLEAR PROTAMINE ZINC INSULIN

A COMPARATIVE STUDY OF THEIR ACTION

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The protamine zinc insulin which has been on the market since February 1937 is only one of many modifications of insulin possible to the chemist. It was selected for general sale and distribution because, of the preparations available at the time, it offered the most in the way of a desirable physical state, stability and an even, prolonged effect. However, work has continued in various laboratories in the attempt to find a preparation which is superior to this modification of insulin. It is our purpose in this paper to report the results which we have observed with three of these newer insulins: histone zinc insulin, globin (zinc) insulin and clear (soluble) protamine zinc insulin.

In common with many clinicians, we regard turbid (market) protamine zinc insulin as a highly satisfactory product. In this clinic its use alone or in combination with crystalline insulin (solution of zinc insulin crystals) or amorphous ("regular") insulin has been, and is, enthusiastically sponsored. With this preparation it has been possible to secure good to excellent control of the condition of most diabetic persons at relatively little inconvenience to the patient. However, it presents certain minor disadvantages: 1. Since it is a suspension rather than a solution, to insure thorough mixing of the contents the vial must be carefully and gently shaken before each dose is withdrawn. If this is not done, accurate sampling of the contents of the vial is not possible. Since the majority of diabetic patients have had little or no scientific training, it is likely that some variation in dosage occurs from day to day, although clinical results indicate that this source of error is relatively slight. 2. It is not indefinitely stable, although the loss in potency proceeds so slowly, even at room temperature, that from a practical standpoint this is of small consequence. 3. Because of its slowness of action, it is often necessary to give an accompanying injection of rapidly acting insulin, either amorphous or crystalline. 4. In patients with severe diabetes it is at times difficult to control glycosuria in the late afternoon and early evening if one follows the usual, convenient plan of giving all insulin before breakfast and none during the rest of the day. 5. Untoward local (allergic) cutaneous responses, although usually mild, are relatively common and at times annoying. 6. A final disadvantage, which can be overcome by careful adjustment of dosage and the giving of a bedtime lunch, is that of hypoglycemic reactions during the night.

Histone insulin is prepared by adding to insulin the simple protein histone, derived from thymus. Although worked with to some extent by Hagedorn and his associates,[1] it was first used in clinical trials by Biasotti, Deulofeu and Mendive [2] and by Gray, Bischoff and Sansum.[3] Both of these groups found that histone insulin has a prolonged action. Recently Barnes, Cuttle and Duncan [4] reported their results with a preparation to which zinc had been added; they found that the hypoglycemic effect of histone zinc insulin, although prolonged, is somewhat more prompt in onset than that of protamine zinc insulin. They conclude that with histone zinc insulin it is "possible to secure a continuously normal blood sugar level and a freedom from glycosuria in a larger number of patients after a single morning injection" than with a single morning injection of unmodified or of protamine zinc insulin.

Globin insulin was first prepared by Reiner, Searle and Lang [5] by combining insulin with globin, a simple protein obtained from erythrocytes by removing the iron-containing chromogen fraction. These workers found that in rabbits the action of globin insulin was more than twice as long as that of regular insulin. In the first report of the use of this preparation clinically, Bauman [6] stated that patients with mild or moderately severe diabetes were adequately controlled on a single daily injection and emphasized that no local cutaneous responses were observed. Since these papers of Reiner and his associates and of Bauman in 1939, reports regarding the use of globin (zinc) insulin have been

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Because of lack of space, this article is abbreviated in THE JOURNAL by the omission of the majority of charts, tables and reports of cases. The complete article appears in the authors' reprints.

The hospital expenses of the patients and the salaries of Mrs. Rita M. Reed and of five part time workers who gave technical assistance were paid by Eli Lilly & Co. and by Burroughs, Wellcome & Co. (U. S. A.), Inc. Histone zinc insulin and clear protamine zinc insulin were supplied by Eli Lilly & Co.; the turbid protamine zinc insulin and crystalline insulin were of market variety and were also supplied without cost by Eli Lilly & Co. The globin (zinc) insulin was supplied by Burroughs, Wellcome & Co. (U. S. A.), Inc., for investigational use. All insulin preparations were stated by the manufacturers to contain 80 units per cubic centimeter.

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2. Biasotti, Alfredo; Deulofeu, Venancies, and Mendive, J. R.: Action of Histone Insulin on the Blood Sugar, Prensa méd. argent. **24:** 1122 (June 2) 1937.

3. Gray, P. A.; Bischoff, Fritz, and Sansum, W. D.: Treatment of Diabetes Mellitus with Insoluble Insulin Compounds: II. Histone Insulin, Ann. Int. Med. **11:** 274 (Aug.) 1937.

4. Barnes, C. A.; Cuttle, T. D., and Duncan, G. G.: Histone Zinc Insulin—Its Pharmacologic Characteristics and Its Application in the Treatment of Diabetes Mellitus, J. Pharmacol. & Exper. Therap. **72:** 331 (Aug.) 1941.

5. Reiner, L.; Searle, D. S., and Lang, E. H.: Insulin Preparations with Prolonged Activity: I. Globin Insulin, Proc. Soc. Exper. Biol. & Med. **40:** 171 (Feb.) 1939.

6. Bauman, Louis: Clinical Experience with Globin Insulin, Proc. Soc. Exper. Biol. & Med. **40:** 170-171 (Feb.) 1939.

made by Marks,[7] by Andrews and Groat [8] and by Bauman [9] in a second publication. More recently Duncan and Barnes [10] announced their results of a study of globin (zinc) insulin on 5 patients; they state that its speed and length of action lie between that of regular or crystalline insulin and that of turbid protamine zinc insulin. They found that the hypoglycemic effect of globin (zinc) insulin begins soon after injection and gradually increases in intensity until between the eighth and the twelfth hour, at which time the effect begins to subside. They believe that, unit for unit, globin (zinc) insulin has a quantitatively greater effect than protamine zinc insulin.

TABLE 1.—*Characteristics of Insulins Studied*

Insulin	Source of Added Protein *	Character	p_H	Composition per 100 Units of Insulin: Added Protein,* Mg.	Composition per 100 Units of Insulin: Zinc, Mg.
Histone zinc	Thymus	Turbid	7.0±	3.2	0.2
Globin (zinc)	Beef blood	Clear	3.7	3.75	0.31
Clear protamine zinc	Salmon sperm	Clear	3.3-3.5	3.8	0.31
Turbid protamine zinc	Salmon sperm	Turbid	7.0±	1.25	0.2
Crystalline	None	Clear	3.0-3.5	None	>0.02 <0.04

* Histone, globin or protamine.

Clear (soluble) protamine zinc insulin was prepared first for clinical trial in 1936 in the Lilly Laboratories by Mr. George B. Walden by adjusting the p_H at from 3.3 to 3.5 and adding more protamine, zinc and glycerin than is present in turbid protamine zinc insulin. It is a water-clear preparation. Although it has been used on a small group of patients in this clinic for more than three years, no statements have heretofore been published regarding the results obtained.

TABLE 2.—*Data Regarding Patients Used as Subjects in Study*

Patient; Sex; Age, Years	Net Weight, Kg.	Net Height, Cm.	Onset of Diabetes	Insulin Dose at Discharge	Diet During Study: Carbohydrate	Protein	Fat	Calories
1 G. T. ♂ 30	58.6 (129 lbs.)	179.5 (71 in.)	1928	8* + 40 †	185	91	115	2,139
2 M. H. ♀ 47	55.0 (121 lbs.)	155.6 (62¼ in.)	1924	40 ‡	152	83	98	1,822
3 D. F. ♂ 22	45.8 (101 lbs.)	147.5 (59 in.)	1928	18 * + 40 †	211	106	122	2,366
4 R. M. ♂ 19	61.8 (136 lbs.)	181.2 (72½ in.)	1928	52 ‡	184	130	133	2,453
5 A. S. ♂ 23	54.0 (119 lbs.)	168.1 (67¼ in.)	1932	80 ‡	152	84	120	2,028

* Crystalline insulin. † Protamine zinc insulin. ‡ Histone zinc insulin.

CHEMICAL METHODS

The determination of blood sugar was made on capillary samples by the micro procedure of Folin and Malmros.[11] Smith's [12] modification of Benedict's method for the determination of the percentage of sugar in urine was used. The total nitrogen in the urine was determined by Folin's [13] micro Kjeldahl method.

PLAN OF INVESTIGATION

Five diabetic patients, 4 men and 1 woman, with moderately severe or severe diabetes, remained in the hospital from seventy-four to one hundred and thirty-two days as subjects for these studies. All 5 patients were known to have had diabetes for more than ten years, with the exception of A. S., who had had the condition nine and three-tenths years. All were intelligent, cooperative, thoroughly reliable and trustworthy and had no significant complications. Four subjects were young, active adult men aged 19 to 30 and 1 was an active woman aged 47.

During the entire study the patients were ambulatory and, as far as practicable, took the same amount of exercise each day. The diet for each patient was kept the same throughout the study as far as the amount of carbohydrate, protein and fat and the total number of calories per twenty-four hours were concerned. The carbohydrate, which varied in amount in different patients from 152 to 211 Gm. a day, while kept constant in total quantity per day was varied from time to time in distribution between meals in order to allow each insulin the most favorable conditions for action.

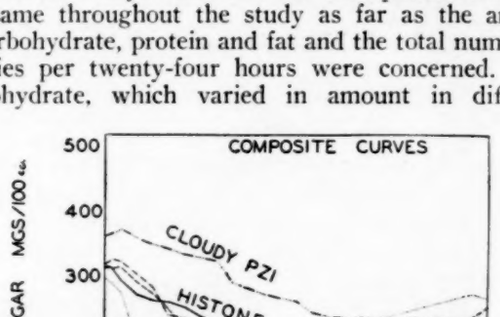

Chart 6.—Composite curves: Each of the curves represents the composite effect of single subcutaneous injections of insulin into the 5 fasting diabetic subjects whose individual curves are shown in charts 1 to 5. The curve for histone zinc insulin is a composite of ten curves, globin (zinc) insulin ten curves, turbid protamine zinc insulin four curves, clear protamine zinc insulin nine curves and crystalline insulin six curves. Blood sugar determinations were made hourly from 8 a. m. until 11 p. m. or 12 midnight anad then again at 7 and 8 a. m. the following morning. No food was given during the test. In 3 cases 0.15 unit of insulin per kilogram of body weight was given on separate days; in 2 cases (A. S. and D. F.) 0.20 unit per kilogram was used. No blood samples were taken between the fifteenth and the twenty-third hour.

The urine was examined qualitatively for sugar at 6:30, 9:30 and 11:30 a. m. and at 2:30, 4:30, 7:30 and 9:30 p. m. daily. In addition, the entire amount of urine voided in twenty-four hours was collected daily and its content of sugar and nitrogen determined.

Except on special test days when hourly samples were taken, blood was obtained for analysis of its sugar content at 7 and 11 a. m. and at 2, 5 and 10 p. m. daily throughout the study. On these days of maintenance the insulin under study at the time was given before breakfast and the patient regulated as well as possible on this single morning dose. The distribution of carbohydrate in the diet was altered slightly from time to time to allow the most favorable action of the insulin under study. Each type of insulin was used from seven to thirty-two days (average fifteen days) by each

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10. Duncan, G. G., and Barnes, C. E.: Globin Insulin, Am. J. M. Sc. **202**: 553 (Oct.) 1941.
11. Folin, Otto, and Malmros, H.: An Improved Form of Folin's Micro Method for Blood Sugar Determinations, J. Biol. Chem. **83**: 115 (July) 1929.
12. Smith, M.: A Micromodification of the Method of Benedict for the Quantitative Determination of Reducing Sugar in Urine, J. Lab. & Clin. Med. **7**: 364 (March) 1922.
13. Folin, Otto: Micro Kjeldahl Colorimetric Method for the Determination of Total Nitrogen in Urine, Laboratory Manual of Biological Chemistry, ed. 5, New York, D. Appleton-Century Company, 1934, p. 145.

patient. Every effort was made to obtain the best possible control with each type of insulin.

In addition to studying the action of each insulin in day by day maintenance, tests were carried out on special fast days during which the patient received no food for about thirty-eight hours. These special test days followed several days of regulation on crystalline insulin to avoid the overlapping effect of the longer acting insulins. As a result, the 8 a. m. blood sugar at the beginning of the test was usually fairly high. After two control blood samples had been taken, the insulin under study (always of U-80 strength) was given subcutaneously with a 1 inch, 27 gage needle and a 0.25 cc. syringe having a scale-bearing portion 3.6 to 5 cm. long divided into ten equal parts. Three patients received 0.15 unit, and 2 (A. S. and D. F.) 0.2 unit, of insulin per kilogram of body weight, thus making the dose 7 to 11 units. Following the injection of insulin, samples of blood for the determination of sugar were obtained at one-half hour, one hour and then at hourly intervals thereafter throughout the day until 11 p. m. or midnight. Hourly tests were then discontinued until 7 and 8 a. m. the next morning when two final determinations were made. Following this, the usual breakfast and insulin were given. During these special test days the patients were confined to the hospital floor and took only water and black coffee or weak tea without milk or sugar. These special test days were at least three and usually five or six days apart, because they were disagreeable for the patient and because he lost from 2 to 7 pounds (900 to 3,175 (Gm.) on those days.

RESULTS

A. *Effect of a Single Subcutaneous Injection of Insulin During a Day of Starvation.*—The accompanying ten charts with their legends show concisely the results of the investigation. Charts 1 through 5 show the level of the blood sugar determined hourly during the fast days on each patient. Besides comparing the actions of the insulins one with another, these graphs compare the experimental insulins with the market turbid protamine zinc insulin and the market crystalline insulin.[14] Each curve represents the composite result of two separate tests done on different days on that patient. Chart 6 represents the composite curves of all the tests on all the patients. The histone curve is a composite of ten tests, the globin of ten tests, the clear protamine zinc insulin of nine tests, the crystalline of six tests and the turbid protamine zinc insulin of four tests.

Histone Zinc Insulin: From a study of charts 1 to 6, it is evident that on fast days the action of histone zinc insulin began approximately one-half hour after subcutaneous injection, and within two hours the blood sugar showed a definite initial fall of approximately 45 mg. per hundred cubic centimeters. This initial action, evident in 4 of the 5 patients (all except M. H.) and due probably to the presence of some soluble insulin in the preparation, may explain why on days of maintenance histone zinc insulin allows less rise in blood sugar following breakfast than globin (zinc) insulin, clear protamine zinc insulin and turbid protamine zinc insulin. Following the initial fall there was a gradual even decrease in the blood sugar until about the fifteenth hour. Since no blood sugar estimations were made from midnight until 7 a. m. the next morning, the exact hour of the night at which the lowest blood sugar occurred cannot be stated definitely. In 3 cases, however, the blood sugar the following morning (twenty-two and one-half hours after injection of insulin) was on the average 41 mg. per hundred cubic centimeters[15] lower than at fifteen hours. A. S., the patient with the most severe diabetes, showed by the twenty-third hour an increase in blood sugar of 65 mg. per hundred cubic centimeters, which would indicate that the lowest level

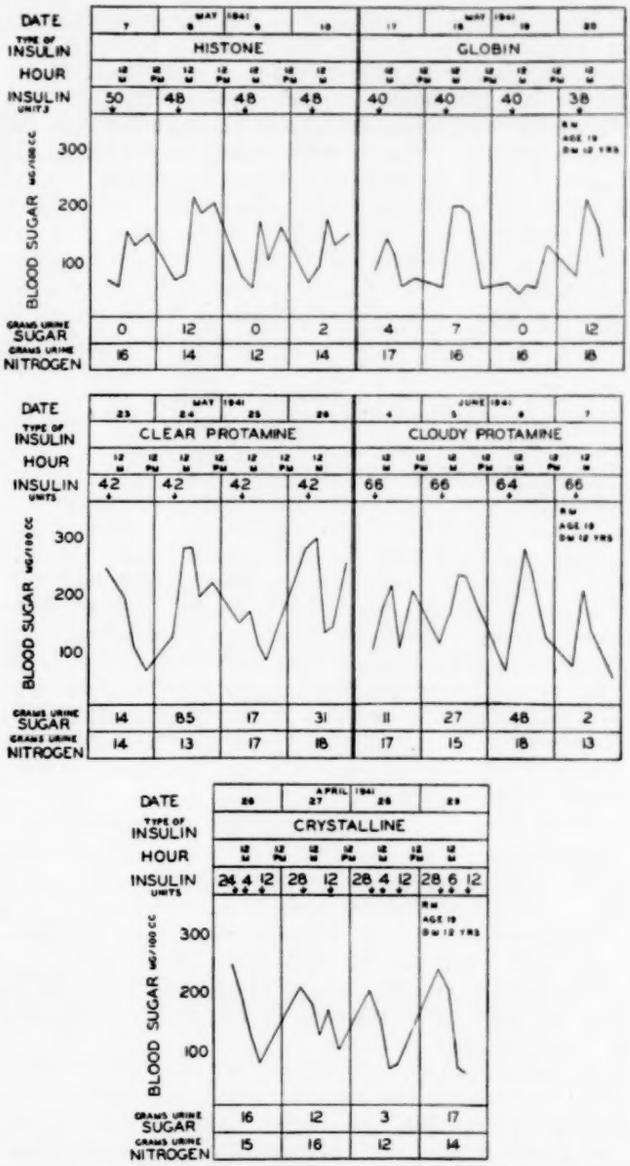

Chart 10 (case 4).—R. M. (for personal data see legend of chart 4). Previous insulin dose was 8 units of crystalline and 36 units of protamine zinc insulin. He was in good health and had no other illness. He remained in the hospital one hundred and four days (March 17 to June 12, 1941) for this investigation. During this study his diet consisted of carbohydrate 184 Gm., protein 130 Gm. and fat 133 Gm., a total of 2,453 calories. The carbohydrate distribution with each of the insulins studied was as follows: histone zinc insulin: 56, 59, 0 (3 p. m.), 59, 10; globin (zinc) insulin: 46, 69, 10 (3 p. m.), 50, 10; turbid protamine zinc insulin: 46, 69, 10 (3 p. m.), 50, 10; clear protamin zinc insulin: 46, 69, 10 (3 p. m.), 50, 10; crystalline insulin: 56, 50, 0 (3 p. m.), 56, 10.

14. Crystalline insulin refers to the market "solution of zinc insulin crystals" and was used as the quick acting insulin in this investigation. Studies made by Marble and Vartiainen (Crystalline Insulin, J. A. M. A. **113**: 1303 [Sept. 30] 1939) and by Ricketts and Wilder (Solutions of Amorphous Insulin and Solutions of Zinc Insulin Crystals, ibid. **113**: 1310 [Sept. 30] 1939) have shown that the action of crystalline insulin and regular insulin are, for practical purposes, identical.

15. We realize fully the danger in quoting here and subsequently in the paper figures obtained by averaging values obtained on only 2 to 7 patients, particularly since the blood sugar is influenced by so many factors. However, since such averages are helpful and significant in indicating gross trends, they are presented for this purpose.

was reached during the night and that the blood sugar was rising. The fact that the rise was slight would indicate that there was still some effect of the histone zinc insulin present twenty-four hours after injection.

Globin (Zinc) Insulin: The onset of action of globin (zinc) insulin usually began in approximately one hour. Thereafter there was a steady and fairly rapid fall in the blood sugar until the eighth to the tenth hour, after which there was a slight and gradual fall until the fifteenth hour (following which blood sugar determinations were discontinued until 7 a. m. the next day) in 3 patients (G. T., M. H., D. F.). In 1 (A. S.) the blood sugar remained constant from the eleventh to the fifteenth hour. In the other patient (R. M.) the blood sugar remained almost constant between the eighth and the fifteenth hour, rising only 15 mg. per hundred cubic centimeters during that period. In all except 1 (G. T.) the twenty-three hour blood value was definitely higher than that at the fifteenth hour, with an average difference of 154 mg. per hundred cubic centimeters. In G. T., the patient with the mildest diabetes, there was a slight drop in blood sugar of 15 mg. between the fifteenth and the twenty-third hour.

From these data, it appears that the greatest action of globin (zinc) insulin occurs in less than twenty-four hours and that its action begins wearing off between fifteen and twenty-four hours after injection.

Clear Protamine Zinc Insulin: The effect of clear protamine zinc insulin was remarkably similar to that of globin (zinc) insulin on the fast days. At approximately one hour after injection there began a steady and moderately rapid drop in blood sugar which in 4 of the 5 patients reached the lowest level in ten to eleven hours. From the tenth to the fifteenth hour the blood sugar remained almost constant except in the case of G. T., whose blood sugar continued to drop slowly during this period. In every case there was a definite rise in blood sugar from the fifteenth to the twenty-third hour, averaging 94 mg. per hundred cubic centimeters for all cases.

B. *Results During Periods of Maintenance.*—Four of the 5 special study patients were given a single daily dose of each of the insulins under study for a total of seven to thirty-two days while on a constant diet. Determinations of the blood sugar were made five times a day. For purposes of analysis we have chosen those three or four days during which the diabetic condition was best controlled on each of the insulins; charts 7 to 10 show these results.

In addition to these 4 patients, we attempted to regulate the diabetic condition of 7 hospitalized patients with histone zinc insulin, 7 others with globin (zinc) insulin and 7 others with clear protamine zinc insulin. These patients received a constant weighed diet, had the quantity of sugar in the urine determined daily and had frequent blood sugar tests taken, but the study was less rigidly controlled than with the 4 original patients.

Histone Zinc Insulin: The diabetic condition of the 4 special study patients maintained on histone zinc insulin was uniformly well controlled with an average excretion of sugar in the urine of only 5 Gm. a day during the periods of best control, as shown in charts 7 to 10. The fasting blood sugar values were almost always well within normal limits, indicating that the insulin given the day before prevented nocturnal hyperglycemia and allowed the patient to begin the day with a normal blood sugar level.

The rise in blood sugar from the fasting level to that at 11 a. m. was slight with histone zinc insulin (charts 7 to 10). This rise, which is usually fairly large when a single dose of turbid protamine zinc insulin has been given before breakfast, averaged only 6 mg. per hundred cubic centimeters with the histone zinc insulin as compared to 100 mg. per hundred cubic centimeters with the turbid protamine zinc insulin on the same patients and under the same conditions of study.

With histone zinc insulin the blood sugar rose between 11 a. m. and 2 p. m. an average of 48 mg. per hundred cubic centimeters, as compared with a similar rise of 56 mg. per hundred cubic centimeters with turbid protamine zinc insulin. Between 2 and 5 p. m. the blood sugar value fell an average of 43 mg. per hundred cubic centimeters with histone zinc insulin as compared with a 67 mg. per hundred cubic centimeters fall with turbid protamine zinc insulin. In 3 of the 4 cases there was an average rise with histone zinc insulin of 31 mg. per hundred cubic centimeters between 5 and 10 p. m. This was followed by a slight and gradual fall in blood sugar throughout the night, resulting in a normal fasting blood sugar. In 1 case (D. F.) instead of a rise in blood sugar between 5 and 10 p. m. there was a fall averaging 36 mg. per hundred cubic centimeters. This was followed by a slight rise during the night, but despite this the fasting blood sugar values were within normal limits.

Globin (Zinc) Insulin: This was next used for regulation of the diabetic condition of the 4 subjects selected for special study. Two patients (G. T. and M. H.) were given three meals and a bedtime lunch daily. The other two (D. F. and R. M.) were given three meals and a lunch containing 10 Gm. of carbohydrate at 3 p. m. but no bedtime feeding. The giving of a lunch in the midafternoon rather than at bedtime unmistakably provided a better distribution of food for globin (zinc) insulin.

The fasting blood sugar was almost always normal when globin (zinc) insulin was used, indicating that the effect of this insulin lasted for approximately twenty-four hours (charts 7 to 10). Between 7 and 11 a. m. there was a sharp rise in blood sugar of all 4 patients, averaging 90 mg. per hundred cubic centimeters; the average rise in the 2 patients receiving no midafternoon lunch was 100 mg. and in the 2 receiving an afternoon lunch 80 mg. per hundred cubic centimeters. From 11 a. m. to 2 p. m. the blood sugar rose slightly in 2 cases (G. T. and M. H.) and fell slightly in 2 (D. F. and R. M.) The average change was a rise of 11 mg. per hundred cubic centimeters.

The change in blood sugar between 2 and 5 p. m. depended on whether or not a midafternoon lunch was given. In the 2 cases in which no lunch was given (G. T. and M. H.) there was a rapid, sharp fall in blood sugar averaging 140 mg. per hundred cubic centimeters. In the 2 cases receiving the midafternoon lunch the average fall in blood sugar was only 27 mg. per hundred cubic centimeters. The great importance of a midafternoon lunch is thus illustrated. There was a further slight fall in blood sugar between 5 and 11 p. m. averaging 26 mg. per hundred cubic centimeters.

It may be stated that the diabetic condition of the patients maintained on globin (zinc) insulin and given an afternoon lunch was well controlled. Glycosuria was absent or slight, and blood sugar values were satisfactory.

Clear Protamine Zinc Insulin: The same 4 patients were given single morning doses of clear protamine zinc insulin in an attempt to regulate the diabetic condition with this preparation. One patient (D. F.) maintained

on three meals alone was the best regulated of the group. Two patients (G. T. and M. H.) took bedtime lunches in addition to their three meals. The fourth patient (R. M.) took a lunch yielding 10 Gm. of carbohydrate at 3 p. m. in addition to the three regular meals. Because of hypoglycemic reactions in the evening, a bedtime lunch was later added.

While the patients were receiving this insulin the fasting blood sugar values were often quite high and regulation of the diabetic condition was difficult. This seemed to indicate that the length of action of clear protamine zinc insulin was less than twenty-four hours. With this type of insulin, the rise in blood sugar between 7 and 11 a. m. was small or large, depending on the height of the fasting blood sugar, averaging 113 mg. per hundred cubic centimeters. The blood sugar fell between 11 a. m. and 2 p. m. with an average drop of 38 mg. per hundred cubic centimeters. From 2 to 5 p. m. there was an average decrease of 112 mg. per hundred cubic centimeters. The latter fall often lowered the blood sugar to hypoglycemic levels. A midafternoon lunch was given to 1 patient (R. M.) and the fall in blood sugar was cut in half. With the use of clear protamine zinc insulin a midafternoon lunch seems definitely indicated. Between 5 and 10 p. m. there was usually very little change in blood sugar values, the average being a negligible rise of 8 mg. per hundred cubic centimeters. During the night there was usually a slight to moderate rise in blood sugar resulting in a relatively high fasting level. A bedtime lunch should not be given with clear protamine zinc insulin if it can be avoided.

Turbid Protamine Zinc Insulin: The market variety of protamine zinc insulin was next given to each of 3 patients under special study. The diabetic condition was controlled as well as possible with a single morning dose of this insulin.

TABLE 8.—*Results Obtained with Histone Zinc Insulin in Case 11*

Date, 1941	Histone Zinc Insulin, Units	Blood Sugar, Mg. per 100 Cc.			Sugar in Urine, Gm. in 24 Hours
		Fasting	11 A. M.	4 P. M.	
July 27	80	...	...	...	41
30	100	...	170	240	42
31	100	147	...	...	65
August 1	110	...	97	190	16
2	120	167	...	...	52
6	120	90	112	110	19

The fasting blood sugar values were uniformly within normal limits and on the four consecutive days of best control the fasting blood sugar of the patients averaged 75 mg. per hundred cubic centimeters. This indicates that protamine zinc insulin acts throughout the night and allows a normal fasting blood sugar level.

Between 7 and 11 a. m. the blood sugar rose an average of 100 mg. per hundred cubic centimeters, indicating that this insulin does not act quickly enough to prevent hyperglycemia after breakfast. From 11 a. m. until 2 p. m. the blood sugar continued to rise; the average increase in the 3 patients was 56 mg. per hundred cubic centimeters. The blood sugar level fell from 2 until 5 p. m. with an average drop of 67 mg. per hundred cubic centimeters and then decreased slightly between 5 and 10 p. m. with an average fall of only 9 mg. per hundred cubic centimeters. With turbid protamine zinc insulin the blood sugar level continued to fall gradually throughout the night, indicating the prolonged action of this type of insulin.

C. *Results of Further Clinical Trial.*—In addition to the 5 patients, each of whom remained in the hospital for several months for this investigation, 21 other patients who remained in the hospital for much shorter periods were given the three insulins under investigation in order to obtain further clinical evidence concerning their action. Five patients were convalescing from infections of the feet and 1 from an infection of the scalp, but no patient had an infection active at the time of the study. One patient had been hospitalized because of a broken hip; the remaining 13 patients had no complications.

Seven patients received histone zinc insulin, 7 globin (zinc) insulin and 7 clear protamine zinc insulin. All 21 received a single daily injection in doses estimated to be adequate for control of the diabetic condition.

TABLE 9.—*Results Obtained with Histone Zinc Insulin in Case 12*

Date, 1941	Histone Zinc Insulin, Units	Blood Sugar, Mg. per 100 Cc.			Sugar in Urine, Gm. in 24 Hours
		Fasting	11 A. M.	4 P. M.	
August 4	70	...	...	202	75
5	80	115	204	196	41
6	90	...	...	...	..
8	90	106	83	130	4
10	90	60	93	...	14

Histone Zinc Insulin: The results obtained with histone zinc insulin were excellent, being comparable to those obtained on the five special study patients who remained a longer time. It was particularly encouraging to note that the diabetic condition of the 5 children, including 1 aged 26 months and 1 aged 11 months, was well controlled with a single dose of histone zinc insulin daily even though in 1 patient the amount was as great as 120 units in a single morning injection.

CASE 11.—B. D., a boy aged 13 years, weighing 48.6 Kg., had had diabetes for eight years. No complications were present. The former insulin dose was 26 units of crystalline plus 34 units of protamine zinc insulin daily, with fair diabetic control. The diet during the study consisted of carbohydrate 200 Gm., protein 100 Gm. and fat 100 Gm., totaling 2,100 calories daily. The carbohydrate distribution was 46, 10 (10 a. m.), 62, 10 (3 p. m.), 62, 10.[16] The results obtained with histone zinc insulin are given in table 8.

CASE 12.—H. K., a boy aged 12 years, weighing 34.1 Kg., had had diabetes for four years. No complications were present. The former insulin dose was 20 units of crystalline and 40 units of turbid protamine zinc insulin daily with poor diabetic control. The diet during the study consisted of carbohydrate 184 Gm., protein 92 Gm. and fat 89 Gm., totaling 1,905 calories daily. The carbohydrate distribution was 35, 10 (10 a. m.), 59, 10 (3 p. m.), 54, 16. The results obtained with histone zinc insulin are given in table 9.

Globin (Zinc) Insulin: With this type the results were even more encouraging than those obtained in the 5 special study patients; the diabetic condition was well controlled on a single morning injection. Among the 21 additional hospital patients, the 7 who received globin (zinc) insulin showed approximately the same degree of rise in blood sugar between 7 a. m. and 11 a. m. as the 7 patients who received histone zinc insulin; it is true, however, that among the patients who received the latter type there were 4 with severe diabetes, whereas only 1 of those receiving globin (zinc) insulin required more than 40 units daily.

16. Indicates that 46 Gm. of carbohydrate was given at breakfast, 10 at 10 a. m., 62 at lunch, 10 at 3 p. m., 62 at supper and 10 at bedtime. A similar method of indicating carbohydrate distribution has been used in the case summaries which follow.

By giving a midafternoon lunch hypoglycemic reactions occurring in the afternoon were eliminated. Only one insulin reaction occurred; this was in case 13 (R. L.) in which 90 units of globin (zinc) insulin was given daily. This reaction occurred at 6 a. m. and thereafter in this case low blood sugar values in the early morning were avoided by giving a small bedtime lunch. This was the only patient receiving globin (zinc) insulin who required a bedtime lunch. The fact that the hypoglycemic reaction occurred at 6 a. m. showed that globin (zinc) insulin was effective for at least twenty-three hours. Only 1 patient, case 19 (G. S., a baby aged 21 months), failed to secure good diabetic control on globin (zinc) insulin.

TABLE 11.—*Results Obtained with Globin (Zinc) Insulin in Case 14*

Date, 1941	Globin (Zinc) Insulin, Units	Blood Sugar, Mg. per 100 Cc.			Sugar in Urine, Gm. in 24 Hours
		Fasting	11 A. M.	4 P. M.	
August 15	30	...	...	...	18
18	30	134	200	153	18
19	32	...	...	...	5
21	32	112	161	92	3
22	32	106	148	...	3

CASE 14.—W. M., a man aged 22, weighing 70.9 Kg., had had diabetes for one year. No complications were present. The former insulin dose was 12 units of crystalline plus 24 units of protamine zinc insulin daily, with good diabetic control. The diet during the study was carbohydrate 161 Gm., protein 86 Gm. and fat 98 Gm., totaling 1,870 calories daily. The carbohydrate distribution was 37, 51, 16 (3 p. m.), 57, 0. The results obtained with globin (zinc) insulin are given in table 11.

CASE 15.—J. S., a woman aged 63, weighing 54.1 Kg., had had diabetes for eight years. She was convalescent following an amputation through the thigh for an infected foot. The former insulin dose was 12 units of crystalline plus 24 units of protamine zinc insulin daily, with good diabetic control. The diet during the study was carbohydrate 137 Gm., protein 60 Gm. and fat 72 Gm., totaling 1,436 calories daily. The carbohydrate distribution was 31, 42, 16 (3 p. m.), 48, 0. The results obtained with globin (zinc) insulin are given in table 12.

Clear Protamine Zinc Insulin: The results obtained with clear protamine zinc insulin in the 7 additional patients whose case summaries follow were in general the same as those observed earlier in the 4 special study patients. In some patients fairly good control of the diabetic condition was possible; in certain others the effect of the single dose given before breakfast seemed to last definitely less than twenty-four hours, so that high fasting blood sugar levels resulted. In such patients, near hypoglycemic values in the late afternoon, despite midafternoon lunches, precluded further increases in insulin dosage. The degree of diabetic control varied from patient to patient and in the same patient from day to day; it was not as even and predictable as with histone zinc or globin (zinc) insulin. The different results obtained with clear protamine zinc insulin as compared with those observed with globin (zinc) insulin are surprising and inexplicable in view of the almost identical response seen following single subcutaneous injections into fasting subjects, as shown in chart 6.

TABLE 12.—*Results Obtained with Globin (Zinc) Insulin in Case 15*

Date, 1941	Globin (Zinc) Insulin, Units	Blood Sugar, Mg. per 100 Cc.			Sugar in Units, Gm. in 24 Hours
		Fasting	11 A. M.	4 P. M.	
August 16	30	...	...	...	0
18	30	154	182	118	0
26	30	108	88	112	0
September 2	30	81	78	...	0

Despite these somewhat unfavorable results it is true that since 1937 we have maintained a small group of patients for varying periods of time (4 patients for one to three years) on clear protamine zinc insulin (U-100 strength) and have obtained good to excellent control of the diabetic condition. This experience has demonstrated that with certain patients this preparation is almost ideal. However, with the majority of patients the effect of a single dose daily does not allow as good or constant control as does histone zinc or globin (zinc) insulin. This is undoubtedly due in part to the somewhat shorter duration of action of clear protamine zinc insulin and it is possible that with injections twice daily a desirable method of treatment could be devised. However, in the interest of simplicity and convenience to the patient, we have concerned ourselves solely with the effect of single doses daily.

TABLE 17.—*Results Obtained with Clear Protamine Zinc Insulin in Case 20*

Date, 1941	Clear Protamine Zinc Insulin, Units	Blood Sugar, Mg. per 100 Cc.			Sugar in Urine, Gm. in 24 Hours
		Fasting	11 A. M.	4 P. M.	
September 3	56	200	...	115	21
4	56	253	241	180	28
5	60	57	220	180	23
8	60	80	64	...	3
9	56	168	165	74	21
11	56	106	131	62	..

TABLE 18.—*Results Obtained with Clear Protamine Zinc Insulin in Case 21*

Date, 1941	Clear Protamine Zinc Insulin, Units	Blood Sugar, Mg. per 100 Cc.			Sugar in Urine, Gm. in 24 Hours
		Fasting	11 A. M.	4 P. M.	
September 3	70	...	...	116	26
4	70	43	118	81	0
5	66	51	...	62	2
6	60	274	...	...	63
7	66	...	...	...	57
8	70	41	120	...	Trace
9	64	179	...	...	19
11	64	116	194	...	34
13	64	323	...	...	46
14	68	...	...	...	56
15	68	55	204	...	..

CASE 20.—T. P., a man aged 20, weighing 54.5 Kg., had had diabetes for ten months. No complications were present. The former insulin dose was 30, 0, 25 of crystalline insulin daily, with fair diabetic control. The diet during the study was carbohydrate 187 Gm., protein 95 Gm. and fat 106 Gm., totaling 2,082 calories daily. The carbohydrate distribution was 46, 54, 18 (3 p. m.), 69, 0. The results obtained with clear protamine zinc insulin are given in table 17.

CASE 21.—V. S., a girl aged 18 years, weighing 50 Kg., had had diabetes for fifteen years. She was convalescing from an infection of a toe. The former insulin dose was 16 units of crystalline and 56 units of turbid protamine zinc insulin daily, with good diabetic control. The diet during the study was carbohydrate 182 Gm., protein 86 Gm. and fat 84 Gm., totaling 1,828 calories daily. The carbohydrate distribution was 37, 62, 16 (3 p. m.), 67, 0. The results obtained with clear protamine zinc insulin are given in table 18.

SUMMARY

The results obtained in this investigation are here summarized. All statements made are based on results obtained with a single subcutaneous morning injection of insulin either before breakfast or at the beginning of a special test day during which food was withheld.

I. *Histone Zinc Insulin.*—1. Histone zinc insulin is a long acting insulin, effective for at least twenty-four hours. A single adequate dose before breakfast produces in almost all patients a normal fasting blood sugar value the following morning. In our patients glycosuria was well controlled.

2. During the first two hours following the injection of histone zinc insulin into a fasting diabetic subject there is a definite though moderate fall in blood sugar, due presumably to the presence of a small amount of soluble insulin in the preparation. This may well explain why there is but little rise in blood sugar between 7 a. m. and 11 a. m. (i. e. following breakfast) with this product. This initial action is well illustrated in chart 6.

3. The action of histone zinc insulin resembles closely that of turbid protamine zinc insulin except for the initial action just described and probably for a slightly less prolonged effect.

4. The tendency of the blood sugar level of patients receiving a single, adequate dose of histone zinc insulin daily before breakfast is to be normal fasting, to rise slightly from 7 to 11 a. m., to have a moderate rise between 11 a. m. and 2 p. m., then to fall moderately between 2 and 5 p. m., to rise slightly after supper from 5 to 10 p. m. and then to fall gradually throughout the night.

5. There were definitely fewer hypoglycemic reactions than with turbid protamine zinc insulin or with protamine zinc insulin and crystalline insulin combined. The few reactions observed were similar to those seen after administration of turbid protamine zinc insulin. There were only four reactions during the seventy-seven days that the 4 special study patients received histone zinc insulin. Two of them occurred between 5 and 6 a. m. and two occurred at approximately 11 a. m.

6. A bedtime lunch is advisable, as with turbid protamine zinc insulin, to prevent nocturnal hypoglycemia.

7. In our small series, histone zinc insulin has seemed especially valuable in the control of diabetes in children. S. K. and M. G., aged 11 months and 26 months respectively, were well controlled on histone zinc insulin.

8. No local cutaneous (allergic) reactions were noticed.

9. One definite disadvantage was discovered: The substance, especially that in the U-80 strength and from lots prepared some months before, tends to clump and to adhere to the neck of the vial. It is hoped that this difficulty can be overcome by the manufacturers.

10. For patients requiring doses of insulin larger than 30 to 40 units daily, a single injection of histone zinc insulin allows better control of the diabetic condition than does a single injection of the turbid protamine zinc variety. If doses of the latter type greater than 30 or 40 units daily are required, supplementary doses of crystalline insulin are often necessary.

II. *Globin (Zinc) Insulin.*—1. Globin (zinc) insulin is also a long acting insulin with a duration of effect somewhat shorter than that of histone zinc insulin or turbid protamine zinc insulin. However, its action appears to extend for approximately twenty-four hours and in adequate dosage this insulin usually allows a normal fasting blood sugar level. Glycosuria was well controlled in all of our patients except 1 baby aged 21 months.

2. The initial action is not as great as with histone zinc insulin but a definite effect is evident within two hours after injection. Its subsequent rate of action lies between that of crystalline insulin and that of turbid protamine zinc insulin.

3. The tendency of the blood sugar following an adequate dose of globin (zinc) insulin is to be normal fasting, to have a moderate rise between 7 and 11 a. m., to rise very slightly or to fall slightly between 11 a. m. and 2 p. m., to fall rapidly between 2 and 5 p. m. if no midafternoon lunch is given and to fall only moderately if one is given, to continue to fall slightly between 5 and 10 p. m. and then to rise slightly from 10 p. m. to 7 a. m. the next morning. The moderate rise in blood sugar after breakfast may be lessened if the insulin is given as long as forty-five to sixty minutes before the meal.

4. There is a tendency to a large rapid fall in blood sugar between 2 and 5 p. m. unless a midafternoon lunch is given. The 2 special study patients who received a midafternoon feeding had a total of six insulin reactions in nineteen days while the 2 patients who received no midafternoon lunch had a total of twenty-three insulin reactions in thirty-seven days. Eighty-six per cent of these reactions occurred in the late afternoon or evening. The 7 additional patients treated with globin (zinc) insulin in the hospital and who received a midafternoon lunch had only two reactions in a total of one hundred and forty-one days. This would indicate that a midafternoon lunch can eliminate nearly all of the late afternoon and evening insulin reactions in patients taking this type of insulin.

5. A bedtime lunch is best omitted to avoid hyperglycemia during the night.

6. Our experience to date has not been extensive enough to comment on the statements of Duncan and Barnes [10] and Andrews and Groat [8] that in the same patient smaller doses of globin (zinc) insulin are required for comparable control of diabetes than when turbid protamine zinc insulin is used.

7. No local cutaneous (allergic) reactions were noticed.

8. The fact that this insulin is a stable, water-clear solution is an important advantage.

III. *Clear Protamine Zinc Insulin.*—1. Clear protamine zinc insulin is a long acting insulin whose duration of effect lies between crystalline insulin and turbid protamine zinc insulin, being apparently less than that of histone zinc or globin (zinc) insulin. It seems to last for about eighteen to twenty-four hours.

2. The blood sugar curves on the fast days, during which a small dose of this product was injected, were remarkably similar to curves obtained with globin (zinc) insulin under comparable conditions.

3. Despite this apparent similarity between clear protamine zinc insulin and globin (zinc) insulin on fast days, we found clear protamine zinc insulin a more difficult insulin with which to control the diabetic condition than globin (zinc) insulin. Glycosuria was only fairly well controlled with this insulin.

4. Following an adequate dose of this type of insulin, a moderately large rise in blood sugar occurred between 7 and 11 a. m. The values usually fell between 11 a. m. and 2 p. m. but rose moderately in 1 instance (D. F.). Between 2 and 5 p. m. there was a large fall in blood sugar if no midafternoon lunch was given

and a moderate fall if the lunch was taken. There was a slight rise between 5 and 10 p. m. and a further slight rise between 10 p. m. and 7 a. m.

5. If this insulin is given from forty-five to sixty minutes before breakfast, the rise in blood sugar after the meal may be lessened. A midafternoon feeding is indicated, as it is when globin (zinc) insulin is used, in order to prevent hypoglycemic reactions in the late afternoon. Three patients received this insulin without a midafternoon lunch for thirty-eight days, during which they had twelve insulin reactions. The 8 patients who had a midafternoon lunch were given this insulin for sixty-one days, during which ten insulin reactions occurred. One patient (P. D.) had seven, five in the first three days while taking this preparation, and obviously they were the result of too large a dose. A bedtime lunch should be omitted in order to lessen the tendency to hyperglycemia the following morning.

6. No local cutaneous (allergic) reactions occurred.

7. Like globin (zinc) insulin, this is a stable, clear preparation.

CONCLUSIONS

Histone zinc insulin, globin (zinc) insulin and clear protamine zinc insulin are all insulins with prolonged action, with duration of effect in the order named. The action of histone zinc insulin is longest, closely approximating that of turbid protamine zinc insulin. It differs from the latter in that (1) it has a slight blood sugar-lowering effect within two hours after injection and that (2) larger single doses may be given without producing late hypoglycemic reactions. It shares with market protamine zinc insulin the disadvantage of being a turbid suspension. Some difficulty has been encountered with clumping of particles of histone zinc insulin and adherence to the neck of the vial.

Globin (zinc) insulin is a water-clear solution, the action of which does not extend over as long a period as that of turbid protamine zinc insulin or quite as long as that of histone zinc insulin but in most patients an adequate daily dose before breakfast will allow a normal fasting blood sugar the following morning. On such a regimen the blood sugar level in the latter part of the afternoon is apt to be low and a reaction result, but these can be avoided by redistribution of carbohydrate to provide a small midafternoon lunch regularly. In our small group of patients no local (allergic) cutaneous responses were encountered either with globin (zinc) insulin or with histone zinc insulin.

Clear protamine zinc insulin, also a solution, produced a response in the blood sugar level of a fasting diabetic subject which closely resembled that of globin (zinc) insulin. The diabetic condition of certain patients has been well controlled over long periods of time with this preparation. However, in other patients we have been unable to control diabetes as easily and as effectively with a single morning injection of this insulin as with comparable injections of the histone zinc or globin (zinc) varieties. This is presumably due to the shorter action of the clear protamine zinc insulin.

We believe that histone zinc and globin (zinc) insulins are highly satisfactory products that can be used to control the diabetes of most patients. We are less sure of the value of clear protamine zinc insulin and believe that further clinical trial is necessary before reaching a final conclusion. With some patients, clear protamine zinc insulin is remarkably effective.

Every effort should be made to simplify rather than to complicate the treatment of diabetes. For this reason the number of insulins on the market should be kept to a minimum, preferably two: a rapidly acting and a slowly acting type. The duration of action of the latter should be at least twenty-four hours. There is much evidence clinically to indicate that the overlapping action of the market turbid protamine zinc insulin, secured because of its duration of effect for more than twenty-four hours, is a distinct advantage since it is an added protection to the patient from acidosis.

We believe that, although in certain of their properties the newer types of insulin possess advantages over turbid protamine zinc insulin, these advantages are not great enough to justify complicating the treatment of diabetes by the introduction of these preparations on the market at the present time. Further work is in progress in an attempt to establish their value more definitely.

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THE ETIOLOGY OF DIABETIC ACIDOSIS

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CINCINNATI

Early in the history of the study of diabetic coma it became apparent that acidosis plays an important part in the production of this syndrome. Subsequently it was demonstrated that this state is due primarily to the accumulation of large amounts of organic acids in the tissues, particularly beta-hydroxybutyric and acetoacetic acids, and that the excretion of these, together with smaller amounts of other organic acids, results in a depletion of base. The loss of base causes a dehydration and intensifies the acidosis and a vicious cycle ensues. For some time minor controversies occurred with reference to the relative importance of the acidosis or the toxic effects of the acetone bodies themselves in the production of the coma. Today the physician is aware that both are important.

In view of the predominant role of the acetone bodies in the development of diabetic acidosis and coma it became of interest to determine the mechanism responsible for the formation and utilization of these acids. The observation that, in addition to diabetes mellitus, starvation and many other situations in which the carbohydrate reserves are depleted are also associated with acetonuria led to the assumption first promulgated by Hirschfeld [1] in 1895 that the acetone bodies are abnormal end products. This was subsequently epitomized by Rosenfeld [2] in the quotation "Fats burn only in the flames of carbohydrate." Knoop's [3] studies on beta oxidation of fatty acids, Lusk's [4] observations on the correlation between carbohydrate oxidation and the appearance of acetone bodies and Shaffer's [5] demonstration that the oxidation of acetoacetic acid in vitro is catalyzed by the presence of dextrose lent credence to the hypothesis that the acetone bodies are incomplete products of fat oxidation.

It was assumed from these and other studies that for the complete oxidation of fatty acids the simulta-

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neous oxidation of carbohydrate was essential and that when this did not occur, either because the tissues could not use carbohydrate or because carbohydrate was not available, the fatty acids were only partially oxidized in the tissues. Thus arose the concept of a quantitative relationship between the oxidation of carbohydrates and that of fats and resulted in the development of the so-called "ketogenic-antiketogenic ratio," which has been used so widely in clinical medicine. This hypothesis provided a basis for the assumption that ketone bodies are manufactured in all tissues of the body, that the diabetic organism cannot oxidize them and that the influence of carbohydrate and of insulin in decreasing the ketosis is due to a restitution or stimulation of acetone body oxidation by some carbohydrate product. This has been the prevailing point of view and is still accepted as such by the majority.

The first intimation that this concept is incorrect can be gathered from studies done in 1910 by Embden,[6] who observed that the isolated liver was the only tissue capable of producing acetone bodies on perfusion with fatty acids. Another major contribution appeared in 1928 when Chaikoff and Soskin[7] demonstrated that removal of the liver from the depancreatized dog results in a drop in the blood acetone bodies, thus implicating the liver as the site of acetone body formation in the intact animal. Studies by Quastel and Wheatley,[8] Jowett and Quastel[9] and Edson[10] with the tissue slice technic favored the possibility that the liver was the site of acetone body formation. In 1936 we demonstrated that the ketosis consequent to the administration of extracts of the anterior pituitary gland was due to the formation of acetone bodies by the liver alone. Thus, whereas acetone bodies appear in the blood of normal animals treated with extract of anterior pituitary, this does not occur when the liver is removed.[11] Today it is generally accepted that the liver is the sole site of acetone body formation in the intact organism.

Much work has been done with regard to acetone body utilization by the peripheral tissues. In 1928 Snapper and Gruenbaum[12] demonstrated that perfused striated muscle of normal animals utilizes acetone bodies. The studies by Chaikoff and Soskin in the same year established that both normal and depancreatized dogs can oxidize acetone bodies. Later, Friedemann,[13] also working with normal and depancreatized dogs, could demonstrate no influence of insulin on the normal rate of acetone body utilization by the muscles. Barnes and Drury,[14] Dye and Chidsey[15] as well as our group[16] have presented evidence along similar lines. The more recent observations of Blixenkrone-Moeller[17] and of Stadie[18] on isolated tissues of normal and depancreatized cats confirm these observations.

Working with eviscerated and hepatectomized rabbits we[19] could not demonstrate any influence of dextrose on the rate of the utilization of acetone bodies by the muscles of fed or fasting animals or of those treated with anterior pituitary. Increasing the rate of acetone body utilization by inducing hypermetabolism in similarly prepared animals likewise revealed no relation between sugar and acetone body utilization.[20] In spite of this evidence, many investigators still persisted in the belief that dextrose is ketolytic and that some correlation exists between the oxidation of dextrose and that of acetone bodies. Hence in 1938, together with Waters and Fletcher,[21] some crucial experiments were performed on the heart-lung preparation in which the amount of dextrose and of acetone bodies in the blood perfusing the heart could be regulated. These experiments revealed that there is no correlation between the utilization of carbohydrate and the utilization of acetone bodies, since the ketogenic-antiketogenic ratios varied from zero to infinity. More recently, employing a technic which permitted the analysis of whole animals, we demonstrated again that sugar has no influence on the oxidation of acetone bodies.[22]

The conclusion that can be drawn from these studies is that the utilization of acetone bodies by the peripheral muscles is not in any way affected by the availability of carbohydrate or of insulin. Yet insulin will alleviate the ketosis which occurs in the diabetic state and carbohydrate will do likewise to the ketosis which occurs in starvation. It is obvious, therefore, that they must produce their effect by acting on the site of acetone body production, namely the liver. That is, dextrose and insulin are not ketolytic but are antiketogenic in their action in that they prevent the formation of acetone bodies.

During the course of our studies we observed that the rate of acetone body utilization by the animal is the same irrespective of whether or not the liver is present, which suggests that this organ does not burn the acetone bodies to any appreciable extent. Thus, although the acetone bodies are made in the liver, they are not used there but are secreted immediately into the blood stream. This conclusion is in accord with the studies of Quastel and Wheatley,[8] of Snapper and Gruenbaum,[23] of Edson,[10] and of others working with isolated liver slices, which indicated that the acetone bodies are not abnormal products of incomplete fat oxidation but perfectly normal end products of fat metabolism in the liver. More recently, Stadie and his collaborators have confirmed these conclusions from their observations on isolated tissue slices.[24]

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In order to present a working hypothesis in explanation of these phenomena it was suggested that a diminution in liver glycogen is the essential prerequisite for an increase in fatty acid oxidation, resulting in an accelerated rate of acetone body formation in the liver and a consequent acetonemia. The fact that insulin induces the retention of glycogen in the liver, while the administration of dextrose stimulates the synthesis of glycogen, adequately explains their antiketogenic actions. By making glycogen available to the liver, the oxidation of fat in this organ is arrested and hence the secretion of acetone bodies into the blood stream ceases.[25] The mechanism whereby depletion of glycogen in the liver induces oxidation of fat in that organ may be referable to the concept that both glycogen and fat compete for the same enzyme system.[10] This enzyme system may have a greater affinity for glycogen, which might explain why it is not available for the oxidation of fat when glycogen is present in adequate amounts. When the glycogen concentration is depleted, the enzyme becomes available for the oxidation of fatty acids.

It is generally acknowledged that the liver of the diabetic organism is poor in glycogen because the rate of the breakdown of glycogen is excessive and that ketogenesis occurs when the glycogen content falls below some critical low level.[25] Accordingly, if it were possible to produce an accumulation of glycogen, even in the absence of insulin, ketosis should cease. Experiments performed by Mann, Bodo and their collaborators[26] revealed that the liver and muscles of the untreated depancreatized dog can make glycogen when treated with adequate amounts of dextrose. This led us to postulate that such treatment should also result in a cessation of acetone body formation. We were able to demonstrate that the intravenous administration of large amounts of dextrose to the depancreatized dog receiving no insulin results in a rapid drop in the concentration of acetone bodies of the blood and urine. When the administration of dextrose is stopped, the acetone bodies again accumulate in the blood.[27] In other words, dextrose can inhibit the formation of acetone bodies even in the absence of insulin if it is administered in amounts adequate for glycogen deposition in the liver.

Conversely, one would anticipate that wherever there is an impoverishment of the liver with respect to glycogen, the susceptibility to ketosis and therefore to diabetic coma would be increased. For example, it is a generally recognized fact that the young child does not retain glycogen as readily as does the adult. Hence it was not surprising to find that in both normal and diabetic children a definite correlation exists between the age of the child and its susceptibility to the ketosis induced by a glycogenolytic stimulus.[28] Likewise, in adult diabetic patients in whom it is known that the glycogen concentration in the liver is relatively low, a stimulus which will cause a further decrease of glycogen will produce ketosis, while in the normal subject the same stimulus is ineffective.[28] These facts all indicate that, instead of facilitating fat oxidation, dextrose actually inhibits it. In other words, dextrose exerts a fat-sparing action[29] just as it is known to exert a nitrogen sparing action.

The question might logically be raised at this point, since acetone bodies are normal intermediaries of fat oxidation and are utilized freely in normal and diabetic muscle, Why does an excessive accumulation of these substances in the blood stream ever occur? The probable answer is that there is a maximum rate at which muscles can utilize acetone bodies, just as there is a maximum rate at which muscles can utilize sugar. Recent studies by our group[30] and by Drury and Wick[31] reveal that there is a positive correlation between the concentration of acetone bodies in the tissues and their utilization up to a certain maximum rate (approximately 7 millimols per kilogram of body weight per hour), beyond which utilization is not increased. Therefore, if the rate of fatty acid oxidation and hence the rate of acetone body formation in the liver exceeds the rate at which the muscles use the acetone bodies, ketosis and consequently acidosis will ensue.

Attempts to produce diabetic coma in the experimental animal generally have not met with success. The completely depancreatized dog deprived of insulin and food does not develop the typical syndrome observed in man but appears to die in a somewhat cachectic state. The ketonemia that occurs in such an animal rarely approaches levels comparable to that observed in man. In the cat, a more severe ketonemia may follow the withdrawal of insulin and food, but here too the syndrome is not the same as that in man. However, severe diabetic acidosis and coma can be produced in the completely depancreatized dog by withdrawal of insulin and food plus the administration of a single dose of phlorhizin. This drug decreases the reabsorption of sugar in the kidney tubules and thereby induces an excretion of large amounts of dextrose. This results in a drainage of sugar from the blood, which in turn induces an increase in the breakdown of liver glycogen. Thus by further depletion of glycogen in the liver of the depancreatized dog it is possible to force ketogenesis to such a degree as to result in the accumulation of large amounts of acetone bodies.[29]

During the past year we have been studying the diabetic syndrome of the depancreatized monkey. Studies in the past indicated that severe diabetes does not develop in the depancreatized monkey; in fact, such animals have been compared with the hypophysectomized-depancreatized dog in which the diabetes is known to be mild. Nevertheless, we have succeeded in producing acidosis in the depancreatized monkey at will. If the monkey, several weeks after pancreatectomy, is deprived of insulin but is permitted to eat food freely, severe acetonemia does not develop. However, if food is also removed, the ketosis is exaggerated and acidosis ensues. Thus, within seventy-two hours after the cessation of insulin and the beginning of a fasting period, 1 monkey was in coma with an acetonemia of 175 mg. per hundred cubic centimeters. This monkey presented the typical picture of diabetic coma as observed in man, i. e. unconsciousness, dehydration,

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31. Wick, A. N., and Drury, D. R.: Effect of Concentration on Rate of Utilization of Beta-Hydroxybutyric Acid by Rabbit, J. Biol. Chem. **138**: 129 (March) 1941.

Kussmaul breathing, tarry vomitus and signs and symptoms of peripheral collapse. Incidentally, it was noted that, just as in man, if insulin is not administered sufficiently early to the unconscious monkey recovery does not occur.[32]

It appears, thus, that, so long as the monkey can take in enough food to provide an adequate storage of glycogen in the liver, the rate of fat metabolism and hence the rate of acetone body formation cannot become sufficiently accelerated to cause an excessive acetonemia, even in the absence of insulin.

Of the many possible factors that have been postulated as being responsible for the development of diabetic acidosis and coma in man, emphasis has been placed on (1) deprivation of insulin, (2) infection and (3) dietary indiscretion. Observations on both man and lower species indicate conclusively that deprivation of insulin is a major factor in the production of ketosis because in its absence retention of glycogen in the liver is impaired and hence oxidation of fat goes on at an accelerated rate. However, in some lower species and even in some diabetic patients, if enough carbohydrate is provided for retention as glycogen in the liver, some decrease in the rate of oxidation of fat can be produced even in the absence of insulin.

In a study of insulin deprivation in human diabetes we[33] found that in one group of patients acetonemia and increasing hyperglycemia developed rapidly and culminated in acidosis and precoma within twenty-four hours, while in the second group a significant acidosis did not develop even after one week. When, in addition to insulin deprivation, carbohydrate in large amounts was administered, two types of responses were again observed. In the first group with the "explosive" type of response, irrespective of how large the amount of carbohydrate ingested, the removal of exogenous insulin still resulted in the rapid development of acidosis. In the second group of patients the slowly developing acetonuria could be prevented by the administration of large amounts of carbohydrate.

The clinical association of diabetic acidosis and coma with the presence of infection is beyond dispute. It may not be difficult to account for this correlation, for it has been demonstrated that the infected animal does not form glycogen from lactic acid as readily as does the normal animal,[34] and that infection increases the breakdown of liver glycogen.[35] Both of these phenomena result in a decrease in the amount of glycogen available in the liver, which in turn induces an increase in the breakdown of fat and protein. Therefore, when the diabetic patient has an infection, what little glycogen reserves are present in the liver become further diminished, and ketosis and acidosis ensue. This can be demonstrated vividly by administering phlorhizin to a diabetic patient suffering from a nonspecific infection. The glycosuria that ensues causes a decrease in liver glycogen and ketosis follows. A similar loss of sugar from a normal subject does not induce ketosis.

With respect to dietary indiscretion, many authors state unequivocally that the ingestion of excessive amounts of carbohydrate is an important factor in "breaking the control" of the diabetic patient and in the development of acidosis. This concept dates back a long time and still has many supporters. The certainty with which opinions are expressed concerning the dangers of a high carbohydrate intake for the diabetic patient is somewhat surprising in view of the fact that this assumption was not put to a test on an experimental basis until recently. We studied a group of patients ranging in age from 15 to 67 years. After their insulin requirements were established and the patients were under good clinical control various regimens were instituted. In some cases the insulin dosage was reduced to a level which would just prevent the development of signs and symptoms of acidosis. Other cases were studied in the complete absence of exogenous insulin. In all cases the fat and protein content of the diet was maintained at a constant level throughout the observations, while the carbohydrate content was increased to the limits of the subject's ability to consume it, which varied from 550 to 1,300 Gm. of carbohydrate a day. It was observed that under these conditions, except for the patients mentioned with the "explosive" response to deprivation of insulin, increasing carbohydrate ingestion resulted in increasing carbohydrate retention. It was noted also that in such cases the acetonuria diminished even though the blood sugar and glycosuria showed a pronounced increase.[33]

Our data as to the effect of an excessive intake of carbohydrate definitely contradict the belief that it is an etiologic factor in the development of acidosis in the diabetic patient. In no instance among more than 30 patients studied was ketogenesis stimulated by excessive carbohydrate intake; on the contrary, an inhibition of ketogenesis was frequently observed. The only factor that invariably accelerated the production of acetone bodies was the withdrawal of exogenous insulin, and even under these circumstances some subjects showed an inhibition of acetone body production when put on an excessive carbohydrate intake. The observation that the higher the carbohydrate intake the greater the amount retained and, consequently, utilized is of significance in the light of the modern tendency to increase the carbohydrate content of the diets of diabetic patients.[36]

These studies indicated also that the sudden development of an excesive blood sugar level in consequence of an excessive carbohydrate intake does not precipitate or even facilitate acidosis or coma, and from that point of view hyperglycemia is not dangerous. In fact our observations suggest that, once the minimal insulin requirements are established, increasing increments of carbohydrate intake, and the consequent hyperglycemia, result in increasing retention of carbohydrate for oxidation and storage, with a consequent diminution of the production of acetone bodies. It must be emphasized that a distinction should be made between hyperglycemia due to a high carbohydrate intake and that due to endogenous sources. In the former, the high blood sugar merely reflects the character of the diet and indicates that an increased amount of substrate is available for deposition in the liver; in the latter, the hyperglycemia represents a disturbance of regulation of such a degree that formation of dextrose and breakdown of glycogen are accelerated. Needless to say, excessive amounts of carbohydrate, such as we used, are contraindicated as a therapeutic procedure because of the

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polyuria and resultant loss of weight on the one hand and the possible danger of pancreatic exhaustion on the other.

CONCLUSION

It may be stated that the most important cause of the development of diabetic ketosis and hence of the consequent acidosis and coma is the impoverishment of the liver with respect to glycogen. It is obvious from the data that excessive carbohydrate intake does not produce such an effect, whereas deprivation of insulin does do so. Similarly, any other phenomenon which will accelerate the depletion of glycogen in the liver, such as hyperthyroidism, hyperpituitarism, hepatitis, infection, surgical procedures, gastrointestinal disturbances, vomiting and so on will result in a secondary acceleration of oxidation of fat and the consequent secretion of acetone bodies into the blood stream in excessive amounts.

AVOIDANCE OF DEGENERATIVE LESIONS IN DIABETES MELLITUS

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Maintenance of life is not sufficient in itself as a goal in the treatment of diabetes mellitus. Insulin has made it easy for the patient with diabetes to survive. Therapy with insulin has such a broad zone of safety that its use tends to encourage a policy of laissez faire on the part of the patient and of the physician. Degenerative changes frequently develop in the diabetic patient who has been led to think that the management of his disease has been adequate. Because of this fact, confusion has arisen as to the essential cause of the sequelae of diabetes mellitus; are they inherent in the disease itself or do they reflect inadequacies in the level of control maintained throughout short or long intervals of the diabetic patient's life?

To make an adequate appraisal of the part played by the disease itself as distinguished from conditions imposed by its noncontrol, it is necessary that test subjects live under a regimen which is as free from unphysiologic conditions as circumstances will permit. One must bear in mind that impaired handling of sugar in the diabetic subject leads to certain perversions of the composition of body fluids, only one of which is the elevation of the level of dextrose in the blood and resultant glycosuria. A physiologic level of control is one which would avoid any degree of hyperglycemia, hypoglycemia or glycosuria and which would conserve the sugar handling function in maximal degree. Presumably if one could accomplish this, all conceivable disturbances of the body due to diabetes would be avoided. Through suitable control of the diet and the proper administration of insulin one can work toward an approximation of that state. Ideal control must be quantitatively as well as qualitatively adequate in all regards if it is to serve its designed purpose. This implies not only that the diet must be adapted to the control of the diabetic state but also that it must be fully adequate for optimum nutrition if a physiologic status is to be our goal. Further, the regimen of management must be dynamic; it must be subject to continued reevaluation and adjustment and must be projected into the patient's future life so that lapses in control will not occur. When dealing with the child subject, the state of childhood must be kept in mind and the special problems imposed by childhood must be met suitably through the course of management. To make all these things possible, one must have the continued and unremittent cooperation of the patient, members of his household and those in his community who in any way are concerned with his pattern of life. Adequate physical and financial facilities must be assured for the maintenance of the prescribed regimen.

No one cognizant with the problems of diabetic care will question the desirability of any of the requisites specified, yet all will realize the unlikelihood that they will be met or even approached by the great majority of patients. Even under the best of auspices, diabetic control will fall considerably short of that outlined and of that which the physician would recommend. In patients following the most exacting regimen, periods of excellent control frequently will be interspersed with others characterized by inadequacy. For long intervals patients may seem none the worse for poor control. Even though they may not appear to suffer from the compromise level of management which they have adopted, this does not justify any one in concluding that they are not being affected adversely by the inadequacies of that compromise as compared with a more physiologic level of control. The effects of poor control of diabetes are cumulative and terminate in serious complications or sequelae which lead to impaired function or to death.

In studying the factors which lead to the development of degenerative changes in the diabetic patient, there are advantages in using the child with diabetes as a test subject. Conclusions derived from the child's condition will be applicable to the adult, because the pattern of the metabolic disturbance is not conditioned by the age of the subject. Moreover, confusion may be avoided in view of the fact that the child does not usually exhibit the degenerative changes which are commonplace during the period of postmaturity. Furthermore, the exaggerated response of the child's organism to abnormal metabolic conditions makes it easier to detect adverse states with him than with the adult subject. In the diabetic child one may be justified in concluding that abnormalities of function or of structure which arise must be related to his regimen of living, to his disease or to the interplay between the two.

When studying the child in this connection one must bear in mind that disturbances of growth or of development represent an analogue to strictly degenerative conditions in the mature patient and must be given the same significance in the analysis. Also some degenerative conditions will occur less frequently in the child than in the adult, notably those affecting the vascular system, possibly because of the greater resistance of young tissue to insult. Nevertheless it seems logical to assume that conditions found to favor the development or the prevention of degenerative states in the child will operate similarly for the adult patient.

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We have had an unusual opportunity to observe the course of the diabetic child under conditions which approximate the ideal as pictured in the foregoing discussion.[1] During the past fifteen years approximately 250 children with diabetes mellitus have been under care of the department of pediatrics. About 150 of them are under recurrent supervision at all times, with several of them in residence in the hospital wards. They are given consideration primarily as children, with measures designed for their normal development and maturation. Practically without exception these patients are medically indigent, committed to the hospital as wards of the state. They may be kept in the hospital as long as their condition makes it desirable or while studies concerning their problems are under way. They may be returned to the hospital for reappraisal or for readmission as often as the staff desires or as occasion requires. Both in the hospital and at home the medical staff retains the initiative; an aggressive policy of control of the disease is maintained, which patients and their parents accept and tend to follow. Through individualized services of medical social workers, local relief and other agencies and the medical staff, facilities for continued home care are assured. Each child is examined and treated at the hospital several times a year as long as his family and the local community choose to continue to use our services. In addition to receiving the usual detailed medical and laboratory examinations each time he returns to the hospital, the diabetic child also is seen in consultation with the ophthalmologist, the otolaryngologist, the pedodontist and the roentgenologist. From the cumulative records the reaction of the patient to his therapeutic regimen and his faithfulness in following it can be projected accurately through his whole period of supervision. Recently facilities have been made available for us to call back to the hospital certain young adult patients who previously were under our care, so that their present status can be evaluated. This report is based on the records of over 250 different children with diabetes mellitus who have been treated in our wards for varying intervals during the past seventeen years.

A total of 69 patients are considered in this review, chosen either because of the prolonged duration of their diabetes or because they presented degenerative lesions or related conditions. Of these 69, 60 had been recognizedly diabetic for five years or longer, and 42 of them had had the disease for not less than ten years. Fifty of the group have been under intermittent observation in our clinic for five years or longer, and 32 of them for not less than ten years. The remaining 19 have been observed over intervals varying from single hospital admissions to periods approximating five years. The same principles of diabetic control were prescribed for all subjects, but the manner and degree of cooperation differed widely within the group. Even with those whose records are among the best, several have had single or repeated intervals of noncontrol. In general the freedom from degenerative changes has paralleled the excellence and continuity of good diabetic control.

The survey has been directed toward the incidence of abnormalities of growth, physique or maturation, and toward the occurrence of degenerative lesions of the liver, vascular system, eyes and teeth. Incidence of these abnormalities has been correlated with the duration of the disease, the nature and continuity of treatment and the cooperation of the subject.

Twenty-eight children showed anomalies related to growth at some time during the course of observation. For example, 17 were of substandard height when first seen in our clinic. Each had been recognizedly diabetic for a significant period at that time, the average duration of the disease in the 17 being three and one-half years at the time of the initial examination. All but 4 of this group grew at a normal rate once the therapeutic regimen had been established. Three of the exceptions failed to follow the prescribed course for any appreciable time. The fourth child had been abnormally small from early infancy, long before she became diabetic, and offered several evidences of pituitary disease. Of the children who were initially small but who subsequently grew at a rate which equaled or surpassed that which is standard for their ages, few were able to overcome their handicap completely and remained smaller than standard throughout their period of observation.

Twelve children in the whole series were so short at their terminal observation that they properly might be termed diabetic dwarfs. Six of these were among those who initially were small; the remainder were subjects who remained in a state of poor control for long periods of time. No child whose management had been even fair for the majority of his period of observation could properly be considered as a dwarf or even as abnormally short. We have had no reason to question the rule that the child whose diabetes is properly controlled and who receives an adequate diet will grow as well as the normal child. When inadequate growth is encountered, fault in the diet or in the manner of control must be assumed and disproved before the diabetes in itself or other endocrine abnormality can properly be postulated as causative.[2]

Eleven subjects were slow in maturation, as evidenced by delay in the development of secondary sex characteristics or the establishment of menstruation. All but 2 of these children also had shown retardation of growth; these 2 were in the second decade when their diabetes became manifest. All children who were slow in maturation were under poor levels of control most of the time. All but 1 reached maturity eventually; the exception was the child with associated pituitary disease. No child who was properly controlled showed delay in maturation.

Disturbances of growth and of maturation, then, seem to reflect prolonged periods of uncontrolled or of inadequately controlled diabetes in these subjects. Shorter periods of noncontrol, however, appear sufficient to produce regional abnormalities. Consideration now will be given to some of these conditions.

Enlargement of the liver was noted in 6 children as an accompaniment of other abnormalities. All were girls, each had been diabetic for several years and each showed impairment of growth and delayed maturation. In each instance the patient was brought back to a proper state of diabetic control some time after hepatomegaly had become apparent, and in each subject the enlargement of the liver subsided coincidentally with

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this. Subsequently, however, management again was allowed to lapse by each of these subjects. At least 3 of the group also developed ocular degenerative lesions. Four of them showed excessive amounts of dental caries.

Two methods of appraisal of the vascular system were available from the routine of examination. The first of these, roentgenograms of the soft tissues of the wrists or ankles, revealed no evidence of arteriosclerosis in any subject. The other, the ophthalmoscopic examination, offered evidence of arterial disease in only 1 subject. This was a girl who was 20 years old when first seen by us. She had had diabetes for eighteen years of her life and throughout that time had never been adequately controlled. Her physical abnormalities included dwarfism, infantilism, albuminuric retinitis with bilateral choked disks, retinal hemorrhages, hypertension, uremia and posterior subcapsular lens opacities.

A second subject who returned to the hospital after several years of noncontrol had rather similar findings, including dwarfism, enlarged liver, infantilism, retinal hemorrhages and edema of the right nerve head (choked disk). Following six months of fairly rigorous control the disk had returned to a normal appearance, the hemorrhages had been reabsorbed and the liver enlargement had subsided. Even though her subsequent control left much to be desired, she went on to maturation, married and was delivered of a normal baby.

Six subjects showed retinal hemorrhages, coincident with variable periods of poor control. In some instances these periods were of only a few months duration. In 1 subject they were recurrent. In general they tended to subside and to disappear with the resumption of suitable control.

Clinically demonstrable diabetic cataracts were observed in 6 children. In each instance they were noted at the initial examination in our clinic. All were subjects in the second decade of life, each of whom had developed clinical diabetes not more than two years prior to the appearance of the cataracts and who had remained in a state of noncontrolled diabetes during that time.

In addition to these obvious opacities of the lens, posterior subcapsular opacities of minor degree were discovered in almost a third of the members of the series. These lesions were detectable only through the use of the slit lamp and the biomicroscope and would not have been discovered with any other form of examination. In each instance their appearance was coincident with a period of noncontrol of the diabetes or followed immediately after it.[3] They are the precursors of the clinically apparent opacity and will terminate as such unless their course is checked. In each instance, however, the announcement of their presence to the patient and his parents and an explanation as to their significance and course led to the resumption of desirable levels of control. Thereafter there was no further increase in lens opacities in these subjects, and their eyes today remain free from functional handicap. Similar lesions have not been found in the eyes of those children whose management has been maintained at a satisfactory level.

In our whole series of children with diabetes mellitus, the rate of progression of tooth decay has been about a fourth as rapid as in the general child population of corresponding age.[4] The dentin at the base of caries initially present tended to become sclerotic and to remain so without further advance of decay as long as the dietary regimen was followed in its entirety and the diabetes remained fairly well under control. Other studies made with nondiabetic children indicate that such arrest of caries is dependent on the establishment and maintenance of optimal nutritional and metabolic status.[5] In contrast with the group as a whole, the subjects who failed to follow the specified dietary regimen showed advance of caries even though their diabetic status seemed fairly well controlled. Among those children whose control was the poorest and who presumably were as lax in following the prescribed diet as they were in controlling glycosuria, the incidence and rate of advance of caries were increased notably. In some subjects caries advanced rapidly for periods of a few months coincidentally with relaxation of control and then became stationary and inactive with resumption of proper management. In general, those who showed persistent and excessive advance of caries also offered other evidences of degenerative conditions or retardation of growth.

SUMMARY

We have concluded from our study of diabetic children that adequately controlled diabetes mellitus does not predispose the child to degenerative diseases or to disturbance of growth. The children who have presented such abnormalities have shown concomitantly prolonged glycosuria with accompanying perversions of their normal physiologic state. The inadequacy of the regimen in these subjects could not have been established through their freedom from outstanding symptoms or from early physical signs of abnormality. If we were to have waited to verify the adequacy of management until physical signs had become apparent, irreparable damage frequently would have resulted. The evidence presented supports the premise that degenerative sequelae of diabetes mellitus represent late results of compromise levels of diabetic control, that they can be anticipated in the patient whose regimen of diabetic control or of diet falls appreciably short of physiologic levels, and that they can be prevented through the maintenance of suitable standards of management.

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4. Boyd, J. D.: J. Am. Dent. A. **27**: 750 (May) 1940.

5. Boyd, J. D.; Drain, C. L., and Stearns, Genevieve: J. Biol. Chem. **103**: 327 (Dec.) 1933; Proc. Soc. Exper. Biol. & Med. **36**: 645 (June) 1937.

Nutrition in War Time.—Overcooking and twice cooking should be avoided as far as possible. Take as an example the effect of heat on cabbage. In the raw state 1 ounce of cabbage per day will protect an adult from scurvy. If the cabbage is boiled for twenty minutes 4 ounces will be required to protect from scurvy, if it is boiled for one hour 10 ounces will be required. If it is boiled with soda for only a short time it will be valueless as a protective against scurvy. Jam, which is made with long heating and stirring of fruits, contains no vitamin C. Marmalade is made from oranges, a fruit which normally contains a large amount of this vitamin, but as a result of the long cooking which it receives its vitamin C content is negligible. Cooking meat or potatoes or other vegetables twice usually destroys all traces of even the more heat stable vitamins, such as vitamin B_1. The water in which vegetables have been boiled should not be wasted because it contains many of the mineral salts of the vegetable; it should be made into a soup, preferably a thick one, with peas, beans, lentils or potatoes; alternatively, it could be made into a gravy and used to pour over meat. —Bourne, Geoffrey: Nutrition and the War, Cambridge University Press, 1940.

IS ADMINISTRATION OF VITAMIN K TO THE NEWBORN OF CLINICAL VALUE?

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Quick [1] in 1937 described a method for the estimation of the prothrombin content of the blood that eliminated both thromboplastin and calcium as unknown factors. In 1939 Owen, Hoffman, Ziffren and Smith [2] reported that the prothrombin content of the blood of the newborn was reduced during the first ten days of life as estimated by a method of their own as well as by Quick's method. As we were studying the blood in the newborn at this time, it was decided to include prothrombin estimations in these observations and also to record any clinical manifestations of hemorrhage that might occur during the newborn period. This study was begun in May 1939. Six months later vitamin K was administered to certain of our newborn group and these observations were continued until May 1941.

PROCEDURE

The control group of normal newborn babies included 627 completely breast fed babies, or 64 per cent, and 355 artificially or partially breast fed babies, or 36 per cent, a total of 982 newborn babies. The group given vitamin K included 539 breast fed babies, or 76 per cent, and 172 artificially and partially breast fed babies, or 24 per cent, a total of 711 newborn babies. These babies were given daily examinations, and any hemorrhagic manifestations were recorded.

Vitamin K was given as soon as the infant reached the nursery. For the first six months of the study 1,000 units of the natural vitamin was given in oil. This was changed to the synthetic form because of ease in administration. The 1 mg. tablet was dissolved in 1 teaspoon of water and given with a medicine dropper. Occasionally a newborn baby would regurgitate the medication. For this reason the infant was observed for half an hour after the vitamin K was given and if regurgitation occurred the amount of 1 mg. was repeated. In 42 of the infants in this group 2 mg. of synthetic vitamin K was given to the mother before the birth of the child. This was given at least five hours before delivery and in such instances none was given to the infant.

In the prothrombin studies, blood was withdrawn from the mother at the time of delivery and from the cord immediately after the birth of the infant. Blood was withdrawn from the baby daily thereafter. These determinations were made on the same baby for consecutive days. No baby is included in this study in which daily determinations were not made for at least five days after birth, the only exception being in infants in which hemorrhagic manifestations developed in which the infant's blood was not being studied. In these instances blood was withdrawn on the day that these first appeared and withdrawn daily thereafter.

Prothrombin determinations were made by the method described by Quick on the plasma of 1 cc. of blood. All blood was withdrawn intravenously in chilled oiled syringes and any sample containing cerebrospinal or tissue fluid was discarded (these precautions are probably unnecessary, but as we were making other determinations at the same time that required such precautions this method was used). Thromboplastin was made from rabbit brain as described by Quick. The potency of this material was tested before each prothrombin estimation and all samples that did not check with normal blood at twelve to thirteen seconds were discarded. Three prothrombin determinations were made on each sample of blood.

The biphase method of Warner, Brinkhous and Smith [3] was used as a check at intervals. This gave a slightly lower prothrombin value on individual samples of blood than the Quick method.

In estimating the coagulation values, the blood was taken from the syringe that was used to withdraw the blood for the prothrombin determinations. It was therefore venous. The capillary tube method of Rudolf [4] was used with the tubes and blood kept at a constant temperature of 80 F.

Vitamin C determinations were made by the method of Abt and Farmer.[5] Both micro and macro methods were used.

RESULTS

The prothrombin values during the first ten days of life are shown in chart 1. In the normal newborn baby this is the average obtained on 356 plasma prothrombin determinations in 55 individual infants. For the newborn baby given vitamin K at birth 268 plasma prothrombin determinations on 40 individual newborn babies, and for the newborn in which vitamin K was given the mother before the birth of the child 82 plasma prothrombin determinations in 15 individual newborn babies.

Table 1 lists the number of hemorrhages in the two groups of newborn babies and table 2 the cerebral hemorrhages. Chart 2 is a spot index of the plasma prothrombin content of the blood in 12 newborn babies that exhibited various hemorrhagic manifestations and contains 88 determinations.

Table 3 gives the mortality of both groups studied and table 4 the mortality of the premature babies of both groups studied.

COMMENT

In the two groups of babies observed there were roughly 12 per cent less completely breast fed babies and 12 per cent more artificially and partly breast fed babies in the control group than in the group given vitamin K. Whether this makes any difference in comparison we do not know. Salmonsen [6] has stated that he observed no hemorrhagic disease of the newborn in over 1,000 infants when given cow's milk formulas during the first two days of life. We were unable to find any difference in either the prothrombin values

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Read at the fifty-third annual meeting of the American Pediatric Society, Hot Springs, Va., May 22, 1941.

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6. Salmonsen, Lief: On the Prevention of Hemorrhagic Disease of the Newborn by the Administration of Cow's Milk During the First Two Days of Life, Acta Pædiat. **28**: 1, 1940.

or hemorrhagic manifestations between the breast fed or artificially fed groups. We were also unable to find any difference in either prothrombin values or hemorrhagic manifestations in the parity of the mother, season of birth, type of delivery (except cerebral hemorrhage) or weight of the baby.

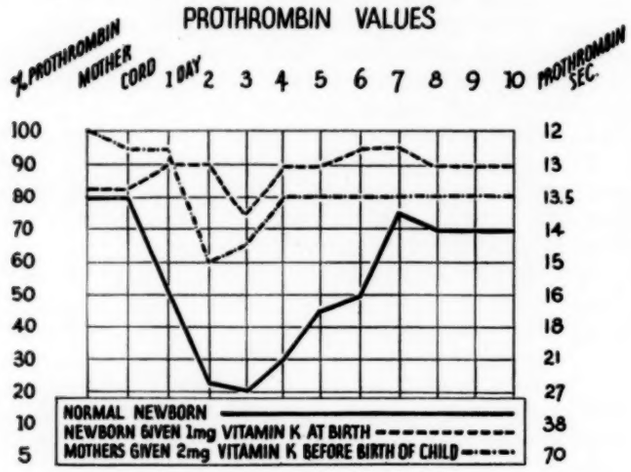
PROTHROMBIN VALUES
% PROTHROMBIN
MOTHER
CORD
1 DAY
2 3 4 5 6 7 8 9 10
PROTHROMBIN SEC.
100 90 80 70 60 50 40 30 20 10 5
12 13 13.5 14 15 16 18 21 27 38 70
NORMAL NEWBORN
NEWBORN GIVEN 1mg VITAMIN K AT BIRTH
MOTHERS GIVEN 2mg VITAMIN K BEFORE BIRTH OF CHILD

Chart 1.—Prothrombin values.

The plasma prothrombin values for the mothers of the control group were consistently around 80 per cent, with similar values for those mothers whose infants were given vitamin K. We could find no differences in parity of the mother or type of delivery. By giving vitamin K to the mother (2 mg. of menadione) this value could be increased 20 per cent. In both the normal control newborn and those given vitamin K at birth the value of the plasma prothrombin in the cord blood was similar to that of the mother. In infants in which the mother was given vitamin K before delivery, cord blood prothrombin was lower than the mother's plasma prothrombin, but as this was considerably higher than untreated mother's, the cord plasma prothrombin was higher than that of the normal infants. It was

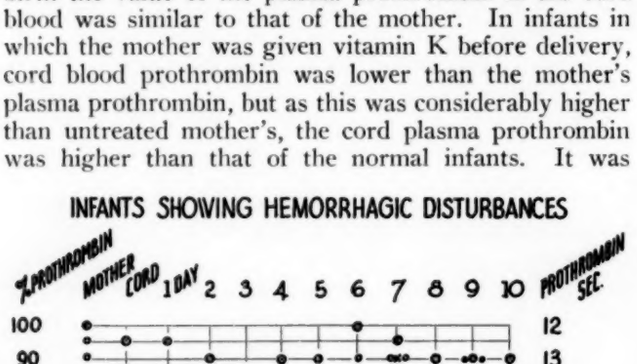
INFANTS SHOWING HEMORRHAGIC DISTURBANCES
% PROTHROMBIN
MOTHER
CORD
1 DAY
2 3 4 5 6 7 8 9 10
PROTHROMBIN SEC.
100 90 80 70 60 50 40 30 20 10 5
12 13 13.5 14 15 16 18 21 27 38 70
UNTREATED INFANTS — x
INFANTS GIVEN VITAMIN K AT BIRTH — o
MOTHERS GIVEN VITAMIN K — o
CEPHALHEMATOMA = 4
MELENA (BOWEL) = 2
HEMATEMESIS = 2
ECCHYMOSIS = 2
CEREBRAL HEMORRHAGE = 2

Chart 2.—Infants showing hemorrhagic disturbances.

found that, to exert any effect on the baby, vitamin K should be given at least five hours before delivery.

In the normal newborn the prothrombin values fall rapidly throughout the first, second and third days of life and rise just as rapidly during the fourth, fifth, sixth and seventh day, and continue at this level for the remainder of the newborn period. Almost all observers [7] are agreed on this decline in the plasma prothrombin value of the blood of the newborn. Infants whose plasma prothrombin did not decrease as much on the first day showed a less total decline by the third day and, conversely, those that showed an early decrease would be lower on the third day. We found two newborn babies in which the prothrombin fell to only 5 per cent on the third and fourth day. One of these showed no symptoms of any kind and progressed normally. The other vomited blood on the third day of life and again on the fifth day when the prothrombin had begun to rise, not on the fourth day at its lowest point.

In the infants given vitamin K at birth this decrease was prevented by an increase in plasma prothrombin values above cord values on the first day, which continued into the second, fell to a little less than cord plasma prothrombin values on the third day, then rose to 10 per cent above cord values on the fourth day and continued during the newborn period at slightly above the value for the normal newborn not given vitamin K.

In the infants whose mothers were given vitamin K before birth the cord plasma prothrombin was about 15 per cent higher than that of the newborn whose mothers were untreated and continued at this value during the first day. On the second day it fell to slightly above the values for the normal newborn. On the third and fourth days it rose to values similar to the cord blood of the untreated newborn and continued as such throughout the newborn period. This is slightly higher than the normal newborn and slightly lower than when the newborn baby was given vitamin K at birth.

TABLE 1.—*Hemorrhagic Manifestations*

Type	Untreated Infants (982)	Per Cent	Infants Given Vitamin K (711)	Per Cent
Conjunctival	21	2.1	12	1.7
Vaginal	11	1.1	8	1.1
Cephalematoma	7	0.7	5	0.7
Petechial and ecchymosis	6	0.6	6	0.84
Cerebral	5	0.5	4	0.56
Hematemesis	5	0.5	4	0.56
Umbilical	5	0.5	3	0.42
Circumcision	3	0.3	3	0.42
Melena (bowel)	3	0.3	2	0.29
Total	66	6.6	47	6.59

Obviously, therefore, there is a marked diminution in the plasma prothrombin content of the newborn baby's blood on the first day of life as compared to cord blood. This decrease continues until the third day of life and then rises to almost cord value by the seventh day and continues throughout the newborn period. It is also evident that this prothrombin content may be considerably increased by the administration of vitamin K to either the mother or the child. Let us now see if any clinical difference between these two groups can be demonstrated.

A word of explanation is necessary in the listing of the hemorrhagic manifestations. Conjunctival hemor-

7. Bray, W. E., and Kelly, O. R.: Prothrombin Studies in the Newborn, Am. J. Clin. Path. **10**: 154 (Feb.) 1940. Fitzgerald, J. E., and Webster, Augusta: Effect of Vitamin K Administered to Patients in Labor, Am. J. Obst. & Gynec. **40**: 413 (Sept.) 1940. Kato, K., and Poncher, H. G.: The Prothrombin Content of the Blood of the Mature and Immune Infant, J. A. M. A. **114**: 749 (March 2) 1940. MacPherson, A. I. S.; McCallum, E., and Haultain, W. F. T.: The Effect of Intrapartum and Neonatal Administration of Vitamin K on the Newborn, Brit. M. J. **1**: 839 (May 25) 1940. Nygaard, K. K.: Prophylactic and Curative Effect of Vitamin K in Hemorrhagic Disease of the Newborn, Acta obst. et gynec. Scandinav. **19**: 361, 1939. Waddell, W. W., Jr., and Lawson, G. M.: Hemorrhagic Diathesis of the Newborn, J. A. M. A. **115**: 1416 (Oct. 26) 1940.

rhages are very common in the newborn. Many newborn babies will show small ones if one looks carefully. Those listed are only the larger ones that exist close to the eyeball and are very easily seen. The same is true of petechial hemorrhages and ecchymosis. Many newborn babies for the first day or two of life will show petechial hemorrhages over the scalp and forehead. Also small bruises are frequently encountered, particularly after a long labor or one requiring instruments. We have listed only petechial hemorrhages if they occurred on the body, and ecchymoses only if the spots were large and not in an area subjected to trauma. Many infants will spit up brown material and hematin crystals during the first day of life. These are not included, but only those that vomited visible blood. Bleeding from the bowel is similar; this does not include stools positive for blood but those in which there was visible blood. Umbilical hemorrhages and circumcisions were listed only if considerable blood was lost, not simple slight oozing.

It will be seen from the number of these hemorrhagic manifestations that occurred in both groups that there is no difference in their frequency. In other words, whether the newborn received vitamin K or not, or whether the prothrombin level is low or not, these hemorrhagic manifestations occur. This is shown by the spot chart of twelve newborn babies that had hemorrhagic manifestations in which the plasma prothrombin

TABLE 2.—*Cerebral Hemorrhage*

Infants Untreated (982)			Infants Given Vitamin K (711)		
Month	Result	Vitamin C	Month	Result	Vitamin C
Aug.	Died (autopsy)	0.25 mg.	Oct.	Died (autopsy)	0.1 mg.
Nov.	Died (autopsy)		April	Died (autopsy)	
July	Recovered	0.03 mg.	Aug.	Recovered	0.3 mg.
Oct.	Recovered	0.2 mg.	Sept.	Recovered	0.25 mg.
June	Recovered				
	Total, 5.....	0.53%		Total, 4.....	0.50%

values were estimated. Only four of these were in a series in which we were studying the blood before the hemorrhage occurred, which accounts for the lack of values for cord blood. The remainder were taken as soon as the hemorrhage was observed. In these infants the value of the mother's plasma prothrombin was estimated on that day instead of at birth. As will be seen in the chart, the values correspond as to whether or not the baby received vitamin K. In the normal newborn the values were low; if vitamin K had been administered, the values were higher. The highest values that we found on any newborn baby were those in which the mother had been given vitamin K before the birth of the child. The prothrombin level was never below 90 per cent, yet this baby had a large cephalematoma, which developed on the second day and increased during the third day. Conversely, one of the lowest prothrombin values that we obtained was in one of the untreated newborn babies in which the prothrombin value on the third day when it vomited blood was only 30 per cent, 20 per cent below normal values. This fell to only 5 per cent on the fourth day with no symptoms. On the fifth day it rose to 15 per cent and the baby vomited blood again. It then rose rapidly to 70 per cent and continued at this value with no more signs of hemorrhage.

We have listed the cerebral hemorrhages separately, as these are the most important of the hemorrhagic group. First we must state that we are never certain of the diagnosis of cerebral hemorrhage. Four infants of both series died and autopsies were obtained. In these the diagnosis was confirmed. In the other 5, all we can say is that in our best judgment they conformed to the accepted diagnosis of cerebral hemorrhage. It will be observed that the frequency is the same for the two groups. All four of the infants that died were delivered instrumentally, and, of the remaining 5, 2

TABLE 3.—*Mortality of Infants During Study*

Untreated Infants (982)	Autopsy	Infants Given Vitamin K (711)	Autopsy
Cerebral hemorrhage.....	Yes	Cerebral hemorrhage.....	Yes
Cerebral hemorrhage.....	Yes	Cerebral hemorrhage.....	Yes
Nuclear icterus.....	No	Erythroblastosis.....	Yes
Atelectasis.....	Yes	Atelectasis.....	Yes
Congenital defect of lung.	Yes	Congenital deformities....	No
Congenital heart.....	Yes	Congenital heart.....	Yes
Hydrocephalus.....	No		
Cause unknown.....	Yes		
Total 8 deaths.....	0.81%	Total 6 deaths.....	0.84%

were delivered instrumentally, 1 was a breach presentation and 2 followed normal deliveries. We have listed the month of these cerebral hemorrhages, as Salmonsen has stated that hemorrhagic disease is most frequent in the spring and late winter, and most infrequent in the summer and fall. This would be a nice point in demonstrating that cerebral hemorrhage is unrelated to hemorrhagic disease, but unfortunately we were unable to find any seasonal correlation either for any of the hemorrhagic manifestations.

We would like to call attention again to the low vitamin C values obtained in these instances of cerebral hemorrhage.[8] In 2 of the infants that died these estimations were by the micro method, which has been questioned, but in the remainder the macro method was used in 3. It did not occur to us to check the vitamin C values in cephalematoma until recently. In the few estimations that have been made, these are also much lower than values obtained for the normal newborn.

In the premature infants studied during the two year period there are almost the same number of infants in each group. All these infants were fed either breast milk or equal parts of breast milk and lactic acid milk. The only hemorrhagic manifestation noted in either

TABLE 4.—*Mortality of Premature Infants During Study*

Premature Infants Untreated (45)			Premature Infants Given Vitamin K (48)		
Lived	Cause of Death	Autopsy	Lived	Cause of Death	Autopsy
1 hr.	Atelectasis.....	Yes	3 hr.	Atelectasis.....	Yes
2 hr.	Atelectasis.....	Yes	8 hr.	Atelectasis.....	Yes
6 hr.	Atelectasis ?.....	No	11 hr.	Atelectasis.....	Yes
8 hr.	Congenital heart.....	Yes	12 hr.	Atelectasis ?.....	No
48 hr.	Atelectasis ?.....	No	14 hr.	Cerebral hemorrhage..	Yes
51 hr.	Atresia of bile ducts...	Yes	30 hr.	Congenital heart.....	Yes
7 days	Congenital deformities	No	8 days	Cause unknown.....	No
	Total 7 deaths.....	15.5%		Total 7 deaths.....	14.5%

group was that 1 of the untreated group passed a stool that contained blood on the third day. We did no prothrombin studies similar to those used on the full term newborn baby. Prothrombin values done on these by micro methods did not give consistent results. All of these premature babies had normal coagulation values for whole blood.

In recapitulation we find that, in our study of 1,693 newborn babies, the percentage of hemorrhagic mani-

8. Fleming, A. W., and Sanford, H. N.: Vitamin C Content of the Blood in Newborn Infants, J. Pediat. **13**: 314 (Sept.) 1938.

festations found in the newborn period was approximately 6.6. These occurred in about equal numbers for the two groups, whether the prothrombin value of the blood was low or high or whether the infants or their mothers were given vitamin K or not. The question at once arises as to whether the quantity of vitamin K administered was sufficient. All we can say is that, in the infants given vitamin K in which estimations were made, its value was above that found in normal infants for the same time of life. These values are also above the accepted values for prothrombin found in other instances of hemorrhage due to prothrombin deficiency. Also in those infants showing hemorrhagic manifestations in which prothrombin estimations were made, high values for prothrombin were found if vitamin K had been given to the newborn baby or its mother, and lower values if it had not been given.

No one has satisfactorily explained these hemorrhagic manifestations that occur in the newborn period with the possible exception of the vaginal hemorrhages found in female infants. These have been assumed to be due to a female hormone reaction. Almost all newborn babies will spit up brown hematin crystals during the first day of life, and Bonar [9] found that 30 per cent of the stools of the newborn were positive for blood. The older clinicians used to classify these hemorrhages into two groups, melena spuria and melena vera. In the former the infant always recovered no matter what treatment was given. In the latter the dread hemorrhagic disease of the newborn developed and the infant's recovery was doubtful.

In the reports of hemorrhagic disease during the newborn period that have been published recently it is apparent that all of these hemorrhagic manifestations have been lumped into the one term "hemorrhagic disease of the newborn," which, it is assumed, is due to a deficiency of prothrombin. We have been unable to show that these hemorrhagic manifestations were associated with a prothrombin deficiency, nor were they lessened by the administration of vitamin K.

We do not believe that these hemorrhagic manifestations are the same thing as true hemorrhagic disease of the newborn. To have a hemorrhage, two things are necessary: (1) a break in a vessel and (2) a failure of the blood to coagulate within normal limits. In none of the instances of hemorrhagic manifestations recorded was the coagulation time of the whole blood increased beyond five minutes. By the same technic the coagulation time of an adult's blood is from five to seven minutes. If these hemorrhagic manifestations are due to a failure of coagulation, one would have to assume that we have a hemorrhage in the newborn baby's blood that coagulates in less time than the coagulation of the adult's blood. This fact and the simple method of testing the coagulation time of the whole blood seem to have been overlooked in the last few years in an endeavor to split up the coagulation factors into components. It has been forgotten that the function of the blood when shed is to coagulate, and that every factor possible is brought to bear to cause this to take place. This is evidently the case in the blood of the newborn. In all adults whose blood we have examined in which a deficiency of prothrombin occurred in levels corresponding to the levels obtained for the newborn for the second, third and fourth days of life, the coagulation time of their blood was decidedly increased (over eight minutes). The newborn baby, therefore, must have a wide margin of safety in all its coagulation elements because it has been found that not only prothrombin but calcium,[10] fibrinogen [11] and platelet disintegration [12] are also diminished. Yet the blood of the newborn coagulates faster than that of the adult.

As we did not encounter an instance of coagulation of the whole blood greater than five minutes in any of these newborn babies, we do not believe that any of these infants suffered from hemorrhagic disease of the newborn. No treatment of any kind was given to the infants in which no vitamin K was given, and no more to the group given vitamin K than the initial administration. This, of course, does not correspond at all to the reports of the frequency of hemorrhagic disease of the newborn recently made, or to the number of infants in which recovery was brought about by the administration of vitamin K.

The explanation of this must lie in two points. Either we do not know what hemorrhagic disease is, or there is a marked difference in our newborn babies as compared to other localities. As to our infants being different, there is that possibility. All of these mothers have had antepartum care, and only rarely do any of our mothers deliver without some antepartum management. As we have found that the prothrombin content of the cord plasma is directly proportional to the prothrombin content of the mother's plasma, we can well imagine that through disease or faulty diet a mother might transmit to her baby a prothrombin content of the plasma that would be low enough to cause serious coagulation difficulties. We have never encountered such a condition, but it could well be. Also we had no congenital syphilis in our group. It has been known for years that syphilitic babies show hemorrhagic tendencies. It has been assumed that this was due to blood vessel disturbance, but it could be due to liver damage and consequently lowering of the prothrombin values. For any of these reasons, babies from mothers delivered without antepartum care might show a larger proportion of hemorrhages.

As to our ability to diagnose hemorrhagic disease of the newborn, the reader will have to decide just what is hemorrhagic disease of the newborn. Clifford [13] states that the frequency of hemorrhagic disease in the newborn is from 1 in 118 to 1 in 333. This included "spontaneous external or internal hemorrhage occurring in the newborn, excluding that associated with trauma, accident or some definite disease." This is approximately a frequency of from 0.3 per cent to 0.85 per cent. On this basis we should consider as hemorrhagic disease our instances of hematemesis and bleeding from the bowel. As these numbered 8 instances in the normal group and 6 instances in the group given vitamin K, this would make our frequency of hemorrhagic disease in the newborn approximately 0.8 per cent, which corresponds to Clifford's values. Waddell and Guerry [14] report "1 case of hemorrhagic disease of the usual variety" and 4 "subclinical hemorrhagic disease" in a series of 60 newborn babies. This makes an incidence of 8 per cent. Our incidence of hemorrhagic

9. Bonar, B. E.: Blood in Stools of the Newborn, Am. J. Dis. Child. **36**: 725 (Oct.) 1928.

10. Bakwin, Harry: Tetany in Newborn Infants, J. Pediat. **14**: 1 (Jan.) 1939.

11. Crane, Marian M., and Sanford, H. N.: Variations of the Fibrinogen Content in the Normal Infant, Am. J. Dis. Child. **51**: 99 (Jan.) 1936.

12. Leslie, E. I., and Sanford, H. N.: Quantitative and Qualitative Studies of Platelets in the Normal Infant, Am. J. Dis. Child. **51**: 590 (March) 1936.

13. Clifford, S. H.: Hemorrhagic Disease of the Newborn, J. Pediat. **14**: 333 (March) 1939.

14. Waddell, W. W., Jr., and Guerry, DuPont, III: The Role of Vitamin K in the Etiology, Prevention and Treatment of Hemorrhages in the Newborn Infant, J. Pediat. **15**: 802 (Dec.) 1939.

manifestations was only 6⅔ per cent; but if we had included more of the smaller conjunctival hemorrhages or perhaps spitting up of hematin crystals, this number could be easily increased to their figures.

On the other hand, Shtern [15] found the condition in 15 newborn babies in 30,627 births, an incidence of 1 in 2,000 infants, and Coppolino [16] 1 in 1,548 births. These discrepancies are due to the definition of hemorrhagic disease of the newborn as interpreted by various authors. Those who report the smaller number of instances consider only those instances of spontaneous hemorrhage in which definite prolongation of the coagulation time of the blood can be shown. On the other hand, those authors who consider cerebral hemorrhage, cephalematomas, conjunctival hemorrhages, spitting up of blood and hematin crystals, cord oozing, petechial hemorrhages, blood in the stool and vaginal hemorrhage as hemorrhagic disease of the newborn will report the greater number.

As stated before, we do not consider any of our infants to have suffered from hemorrhagic disease of the newborn because their coagulation values were within normal limits. This is not surprising, because in the last ten years our frequency of hemorrhagic disease of the newborn by such standards has been 1 in 2,500. Again, if we are failing to diagnose hemorrhagic disease of the newborn our last point is that we should, according to the numbers of infants that have been reported as having been cured of this dread condition, have a considerably higher mortality in our untreated infant group over the group given vitamin K. As will be observed in table 4, the mortality of the two groups of infants is practically the same. There were no internal or external hemorrhages with the exception of the cerebral hemorrhages in either group of infants that died.

The most important point in this entire problem is that of cerebral hemorrhage and its association to hemorrhagic disease of the newborn. We have never observed a cerebral hemorrhage associated with hemorrhage elsewhere in the newborn or in any increase in coagulation values of the whole blood. We were able to estimate prothrombin values in only 2 of our 8 cases of cerebral hemorrhage. In the infant given vitamin K at birth it was high, and in the 1 untreated lower, but not lower than in the normal newborn baby. In all of these cases of cerebral hemorrhage the coagulation of the whole blood was less than five minutes. It is only fair to state that only 4 of these were proved by autopsy, and that in each of these the lesion was a tear through the tentorium. No other signs of hemorrhage in the body were found. The one premature infant that died of cerebral hemorrhage had the same pathologic condition. On the other hand, Salmonsen [17] states that he has found instances of cerebral hemorrhage associated with coagulation prolongation and hemorrhagic disturbances.

While we found no difference in the number of instances of cerebral hemorrhage in our infants treated with vitamin K and untreated infants, we do not feel that our instances of cerebral hemorrhage are large enough to dismiss definitely this form of therapy. As we have no specific therapeutic treatment for this condition at the present time, and as we have found that vitamin K by mouth will raise the prothrombin value of the newborn blood within four hours from administration, it certainly would do no harm to administer vitamin K to any infants suspected of such a condition. Certainly this is much superior to giving them small intramuscular injections of whole blood, which could not possibly have any value except the psychic effect on the parents.[18] We would also recommend giving infants suspected of cerebral hemorrhage vitamin C. While our frequency of cerebral hemorrhage is relatively low, we have found blood vitamin C consistently low in newborn infants with cerebral hemorrhage for the last five years.

In our premature infant studies, while only one infant in the untreated group showed any hemorrhagic tendencies, and this one recovered spontaneously, we again feel that 98 premature infants is hardly enough from which to draw any definite conclusions. None of these premature infants had coagulation values of over five minutes. Micro methods of estimating prothrombin on these premature infants we did not find satisfactory; so we can make no statements about these values, but certainly from the coagulation values of the whole blood no differences were found over the full term infant. The mortality was practically the same for the untreated and the treated group, and the only cerebral hemorrhage in either group was in the group given vitamin K (table 4).

It is unfortunate that we did not encounter any infants with abnormal coagulation functions, such as those reported in which no prothrombin can be found or those in which the coagulation of the whole blood is greatly prolonged. It seems to us that it is rather unnecessary to estimate prothrombin values in the newborn under the average clinical conditions unless there is a prolongation of the coagulation time of the whole blood, which can be shown by simple methods. If such a prolongation exists, its cause can be determined.

CONCLUSIONS

One thousand, six hundred and ninety-three newborn infants were observed during the first ten days of life, over a period of two years. Vitamin K was administered to 711 of these infants. In 606 plasma prothrombin determinations it was found that the prothrombin content of the cord blood plasma of the normal infant was similar to the prothrombin content of its mother's blood plasma. During the newborn period the plasma prothrombin diminished during the first, second and third days of life in descending proportions. It increased during the fourth, fifth and sixth days of life and almost returned to cord value from the seventh day throughout the newborn period. The value of plasma prothrombin could be increased above cord plasma prothrombin value by the administration of vitamin K to the infant. The plasma prothrombin of the mother and the cord plasma prothrombin of her infant were both increased above normal values by the administration of vitamin K to the mother before the birth of her child. The plasma prothrombin values of infants given vitamin K or given to their mothers before delivery is well above that of normal infants throughout the newborn period.

However, the administration of vitamin K did not affect the frequency of hemorrhagic manifestations. There were just as many conjunctival, vaginal, petechial, cerebral and umbilical hemorrhages, cases of melena

15. Shtern, I. A.: Symptomatology, Therapy and Prophylaxis of Melena Neonatorum, J. rann. detsk. vozr. **12**: 396 (Nov.) 1932.
16. Coppolino, J. F.: Hemorrhagic Disease of the Newborn, Atlantic M. J. **31**: 300 (Feb.) 1928.
17. Salmonsen, Lief: Morbus Hemorrhagicus Neonatorum, Acta pædiat. **27**: 1, 1939.
18. Sanford, H. N., and Leslie, E. I.: Hemorrhagic Disease of the Newborn and the Value of Intramuscular Injections of Blood, J. Pediat. **12**: 16 (Sept.) 1938.

and cephalematomas in one group as in the other. The percentage of mortality for the two groups was the same.

There were no hemorrhagic manifestations in either group in which the coagulation time of the whole blood was increased over normal (five minutes). As judged by this standard, our frequency of hemorrhagic disease of the newborn for the last ten years has been one in twenty-five hundred.

952 North Michigan Avenue.

A COMPARATIVE STUDY OF FIBRILLATION AND TREMOR

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This study was undertaken in an effort to ascertain whether or not the coarse fibrillation seen in the skeletal muscles of man is in the same category as tremor and to learn what factors influence it. The term "coarse fibrillation" is used advisedly in order to avoid confusion with the type of fine muscle action which physiologists call "fibrillation." Denny-Brown and

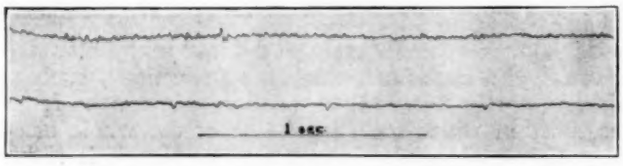

Fig. 1.—Surface solder electrode recordings from lip (upper) and platysma (lower), showing the absence of fibrillation during rest.

Pennypacker [1] have studied a type of fine muscle contraction following complete muscle denervation. These fibrillations are invisible through the skin. They call these contractions "true fibrillations" and refer to the fibrillations visible through the skin as "fascicular contractions." In this paper we are dealing with the phenomenon of irregular muscle contractions visible through the skin as "rippling," which clinicians have called fibrillation.

Brain [2] states: "Fibrillary twitching of muscles is seen in its most typical form as a result of chronic degeneration of the anterior horn cells." This is generally accepted. In what particular way fibrillation is related to damage to neurons is not clear. Russel, Odom and McEachern [3] state that fibrillations occur totally independent of nervous control; they have shown that peroneal nerve block does not stop fibrillation in the distal part of the leg.

Tremor has been studied by one of us,[4] and the following conclusions were reached:

1. Tremors of all kinds have a common pathophysiologic basis. They are regarded as muscular responses to rhythmic discharges in various motor cells in the central nervous system.

2. The so-called physiologic tremor can be obtained in a normal person after "overinnervation," e. g. clenching the fists with utmost force. Since this is a purposive act, it is likely that the motor cortex cells give rise to the rhythmic discharge seen as physiologic tremor.

After alteration of motor cells by disease, degeneration or intoxication, the threshold of neuron discharge is lowered and a minor innervation may produce rhythmic discharges resulting in tremor. The prototype of this pathologic tremor is found in paralysis agitans. Such a patient may shake all day but the tremor always stops during sleep. If, however, some slight stimulus is administered during sleep without awakening the patient, the tremor reappears briefly. In this way the dependence of tremor on stimulus from the outside is shown.

3. The rate of tremor is dependent on the location of the discharging cells in the central nervous system. The rate of 9 to 15 vibrations a second is typical for tremor originating in the cerebral cortex. The so-called physiologic tremor and the tremors of alcoholism, thyroid disease and dementia paralytica are examples of tremors of this high rate. Tremor originating in the corpus striatum has a rate of 5 to 6 a second, as in Parkinson's disease, tumor or other lesions of the motor cells of the corpus striatum. Tremor originating from discharging motor cells of the nucleus ruber occurs at the rate of 3 to 4 a second, as pointed out in the case of a patient with Benedikt's syndrome. Cells of the anterior horn of the spinal cord discharge at the rate of 6 to 7 a second. Its rhythmic muscular effect, however, is not called "tremor" but "clonus." In cerebellar lesions, adventitious movements simulating a tremor are known. Mechanographic recording reveals that this phenomenon is mostly arrhythmic and therefore not a tremor.

METHOD

Fibrillations were studied in 2 cases of progressive muscular atrophy. In the present study tremor was studied in 3 cases of Parkinson's syndrome. Forty-one experiments were performed. Potentials were recorded

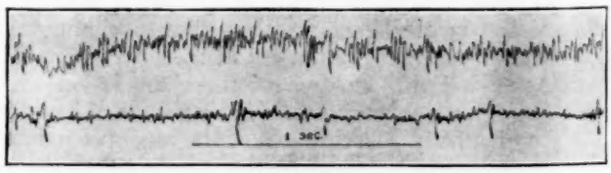

Fig. 2.—The same as figure 1, showing muscle activity in the lip record and fibrillations in the platysma record when the subject protrudes his tongue.

by an ink-writing oscillograph. In the first experiments, two solder disks applied to the skin with celloidin solution were used as electrodes. In later experiments, coaxial needles, which were made according to the method described by Adrian and Bronk,[5] were inserted into the muscles in order to record potentials from single motor units.

The results of the two methods are the same, but the latter method gives a somewhat more detailed picture of muscle activity.

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1. Denny-Brown, D., and Pennypacker, J. B.: Fibrillation and Fasciculation in Voluntary Muscle, Brain **61**: 311-334 (Sept.) 1938.

2. Brain, W. R.: Diseases of the Nervous System, New York, Oxford University Press, 1933, p. 13.

3. Russel, C. K.; Odom, G. L., and McEachern, Donald: Physiological and Chemical Studies of Neuromuscular Disorders, Tr. Am. Neurol. A. **64**: 120-124, 1938.

4. de Jong, Herman: Action Tremor, J. Nerv. & Ment. Dis. **64**: 1-11 (July) 1926; Phénomènes rhythmiques du système nerveux normal et malade, Rev. neurol. **1**: 367-377 (March) 1928. de Jong, Herman: Physiological and Psychological Tests in Tremors and Related Phenomena, Nederl. tijdschr. v. geneesk. **1**: 472-474 (Jan. 28) 1928. de Jong and Schaltenbrand.[6] de Jong and Herman.[7]

5. Adrian, E. D., and Bronk, D. W.: The Discharge of Impulses in Motor Nerve Fibers: II. The Frequency of Discharge in Reflex and Voluntary Contractions, J. Physiol. **67**: 119-151 (March) 1929.

RESULTS

I. *Effect of Muscle Activity.*—A. One patient with progressive muscular atrophy showed very little fibrillation in the right sternocleidomastoid, platysma, tongue and digastric muscles at rest. After the tongue was protruded many gross fibrillations were recorded in these muscles as well as some involuntary contractions of the large fascicular type (figs. 1 and 2). Voluntary contraction of the leg muscles did not produce an increase in fibrillation in the muscles tested. In the second patient this effect of muscle activity on fibrillations was also observed but to a lesser degree than in the first patient.

B. In a patient with parkinsonian tremor, muscular contraction may stop tremor in the contracting muscle but may increase tremor in other muscle groups.

II. *Effect of Tapping.*—When a fibrillating muscle is tapped, fibrillation may increase in it or reappear if it has stopped temporarily. Tapping a normal muscle does not provoke fibrillation. Tapping has no effect in tremor.

found to increase the number of fibrillations. The following protocol illustrates this:

Sept. 6, 1940 needle electrodes were placed in the flexor carpi ulnaris and brachioradialis muscles. Fibrillations occurred arrythmically at the average rate of 12 in five seconds during the resting period. Six minutes after the injection of prostigmine methylsulfate 1.5 mg. combined with atropine sulfate 1 mg., fibrillations averaging 13 in five seconds were visible. Ten minutes after the injection, fibrillations averaged 35 in five seconds (figs. 3 and 4).

B. Prostigmine methylsulfate did not exert any effect on tremor, as illustrated by the following protocol:

Jan. 14, 1941 solder electrodes were placed over the first interspace of the hand, at the flexor carpi radialis muscle, and an indifferent electrode was placed over the styloid process of the radius. Tremor rhythm of about 5 vibrations a second was recorded. The mechanogram was shown as well as the electromyogram. The minimum amplitude of tremor was present when the hand was placed on a pillow. In a more active position (hand on arm of chair) the tremor was more pronounced, whereas it gained a maximum if the left arm was held in a half bent position in the air.

Fig. 3.—Needle electrode recording showing fibrillations in an arm muscle. The distance between the heavy vertical lines is one-half second.

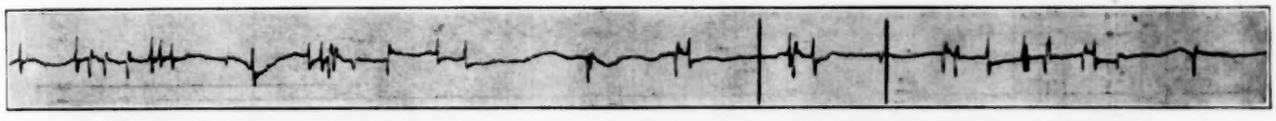

Fig. 4.—The same as figure 3, after injection of prostigmine methylsulfate. A definite increase in the amount of fibrillations is evident.

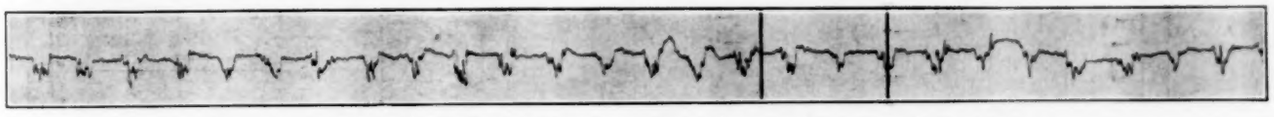

Fig. 5.—Needle electrode recording showing tremor and mechanogram in a case of paralysis agitans.

III. *Effect of Sensory Stimulation.*—A. In fibrillation, no effect on the amount, frequency or intensity of fibrillation was observed as the result of touching or of pricking the skin at any point on the body. Smells, loud noises and the sudden appearance of bright light were ineffective in changing the amount of fibrillation. The application of an ice cube to the skin yielded uncertain results.

B. Sensory stimulation of all kinds may increase tremor, as stated in former publications.

IV. *Effect of Emotion.*—A. In fibrillation, when quick, threatening movements were made in the direction of the face or eyes no increase in fibrillation was noted. Mental arithmetic, which produced some degree of anxiety when the task was of sufficient difficulty, was never observed to produce any definite effect on fibrillation.

B. The same emotional stimuli usually increase the amplitude of tremor.

V. *Effect of Drugs.*—1. Prostigmine methylsulfate: A. In fibrillation, prostigmine methylsulfate in amounts of 1.5 mg. given intramuscularly (with atropine 1 mg. to avoid an unpleasant side reaction) was uniformly

At 10 a. m. an injection of prostigmine methylsulfate 1.5 mg. and of atropine 0.6 mg. was made. Immediately after the injection an increase in amplitude occurred, apparently owing to an emotional reaction from the injection since it appeared immediately after the injection.

At 10:15 a. m. the emotional reaction diminished on the record and reached the same level at which it stood before the injection. If the hand rested on the pillow, tremor again reached a minimum.

At 10:30 a. m. the tremor stopped almost completely. Later on it reappeared when the patient had the "arm half-bent" after he had been talking, as before the injection. No effect of the prostigmine methylsulfate was noted.

2. Barbiturate: A. Soluble pentobarbital 0.2 Gm. was given by mouth on several occasions. No change in the amount of fibrillation could be made out during the waking or sleeping states. On one occasion when the patient was drowsy a hypnotic trance was induced. Here also no change in fibrillation was noted.

B. After soluble pentobarbital 0.2 Gm. the patient became very drowsy, but there was no change in the tremor record. In forty-five minutes the patient was sleeping soundly; no tremor could then be recorded. Noise was made by scratching on the wire of the

Faraday cage and the tremor reappeared, at first with small amplitude and later with normal amplitude. The motor of the apparatus was shut off to reduce the barrage of auditory stimuli. After a minute another record was taken and no tremor could be recorded. The patient was awakened, whereupon the usual tremor record was obtained. This experiment of recording tremors of the sleeping, being stimulated and awakening was repeated three times, always with the same effect; namely, absence of tremor during sleep and reactivation of tremor during sleep by auditory stimuli. That it was not the drug but the state of being asleep which caused the tremor to disappear is obvious, since the drug was active during the interval between these experiments (figs. 5 and 6). The same result was obtained during natural sleep.

3. Bulbocapnine phosphate: A. Bulbocapnine phosphate 75 mg. given intramuscularly had no effect on fibrillation.

B. de Jong and Schaltenbrand [6] found that bulbocapnine suppressed tremor in some patients for a time but was ineffective in other patients.

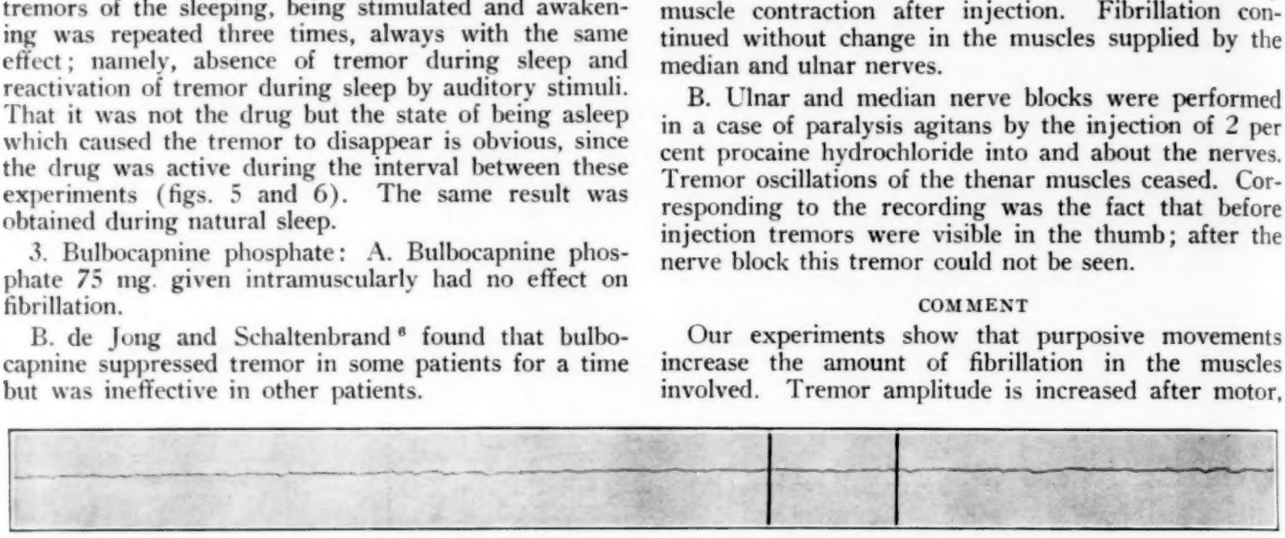

Fig. 6.—The same patient as figure 5. The record shows no tremor because the patient is asleep.

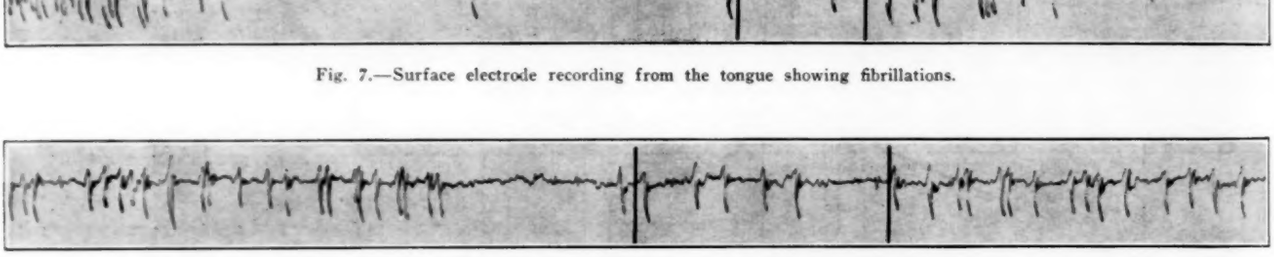

Fig. 7.—Surface electrode recording from the tongue showing fibrillations.

Fig. 8.—The same as figure 7, showing the persistence of fibrillations after scopolamine 0.3 mg. intramuscularly. The space between the heavy vertical lines is one second.

4. Scopolamine hydrobromide: A. Fibrillation persisted after the intravenous injection of scopolamine hydrobromide 0.3 mg. (figs. 7 and 8).

B. Tremor disappeared completely after injection of scopolamine. The following protocol illustrates this.

10:00 a. m., record shows regular tremor.

10:04, scopolamine hydrobromide 0.6 mg., given intramuscularly.

10:09, tremor somewhat diminished.

10:15, tremor absent. Record shows smooth line. Patient is awake and clenches fist in response to command. On inspection of the patient no tremors can be seen anywhere.

10:22, patient asleep. Record shows smooth line.

This protocol shows that the response obtained is due to scopolamine and not to the influence of sleep, in contrast to the results obtained with soluble pentobarbital. Experiments by de Jong and Herman [7] have shown that other pharmacologic agents such as phenobarbital and atropine have no such arresting influence.

VI. *Nerve Block.*—A. The ulnar nerve was blocked at the elbow by the injection of 2 per cent procaine hydrochloride into and about the nerve. Galvanic stimulation of the skin over the nerve that produced a muscle reaction before the injection failed to cause any muscle contraction after injection. Fibrillation continued without change in the muscles supplied by the median and ulnar nerves.

B. Ulnar and median nerve blocks were performed in a case of paralysis agitans by the injection of 2 per cent procaine hydrochloride into and about the nerves. Tremor oscillations of the thenar muscles ceased. Corresponding to the recording was the fact that before injection tremors were visible in the thumb; after the nerve block this tremor could not be seen.

COMMENT

Our experiments show that purposive movements increase the amount of fibrillation in the muscles involved. Tremor amplitude is increased after motor, sensory and emotional stimulation. Prostigmine methylsulfate decidedly increases the amount of fibrillation, whereas this drug exerts no effect on tremor. Fibrillation persists after blocking of the ulnar nerve during sleep and after the injection of scopolamine hydrobromide.

Our experiments confirm the observations of Russel, Odom and McEachern concerning the effect of prostigmine methylsulfate on fibrillation and the persistence of fibrillation after nerve block. The conclusion of these authors is that fibrillations are of peripheral origin and "not due to disordered impulses coming down from anterior horn cells." Grund [8] found that fibrillations persisted during spinal anesthesia.

Denny-Brown and Pennypacker concluded from their experiments that hyperexcitability of the motor neuron, in progressive muscular atrophy or amyotrophic lateral sclerosis, for example, results in periodic discharges of single impulses by the motor neuron and that the focus of discharge is not the synapse but within the neuron.

The interpretation of our experiments leads us to the following conclusion: in muscles whose nerve sup-

6. de Jong, Herman, and Schaltenbrand, G.: The Action of Bulbocapnine on Paralysis Agitans and Other Tremor Diseases, Neurothérapie **6**: 61-72, 1924.

7. de Jong, Herman, and Herman, William: The Action of Bulbocapnine in Three Cases of Paralysis Agitans and in One Case of Tremor of Paralysis Agitans Type: A Further Note with a Comparison of the Action of Scopolamine, Atropine and Phenobarbital, Arch. Neurol. & Psychiat. **16**: 55-62 (July) 1926.

ply is slowly degenerating, fibrillation may occur independently of the central nervous system. However, since impulses for voluntary movement may increase fibrillation, it is clear that impulses coming down from the central nervous system may exert an influence on fibrillation.

The accompanying table shows the differences observed between fibrillation and parkinsonian tremor.

On the basis of these differences, it is clear that fibrillation and parkinsonian tremor are phenomena of different natures. In previous publications one of us (de J.) demonstrated that rhythmic phenomena of the central nervous system, such as tremor, must be regarded as the muscular effect of rhythmic discharges in motor nerve cells of different levels of the central nervous system. These rhythmic discharges are induced and influenced by afferent impulses. The evidence for this has consisted up to this time in experiments on patients with paralysis agitans in whom tremor which had ceased completely during natural sleep, as recorded by a mechanogram, could be reactivated by stimuli

Differences Between Fibrillation and Parkinsonian Tremor

Fibrillation	Tremor
Arrthymic	Rhythmic
Irregular rate	Constant rate
Present during sleep	Absent during sleep
Present after scopolamine hydrobromide	Absent during scopolamine hydrobromide
Present after bulbocapnine phosphate	May be absent after bulbocapnine phosphate
Increased after prostigmine methylsulfate	Not affected by prostigmine methylsulfate
Present after nerve block	Absent after nerve block
Activated by impulses for voluntary movement	Activated by all stimuli
Activated by mechanical stimulation of muscle	
Not affected by pinprick, cold or emotion	

without waking the patient. This indicates that tremor is of central origin. Considering the facts presented in the table, it is obvious that fibrillation cannot be of central origin.

Filbrillation appears to be secondary to long continued, slow destruction of the anterior horn cells but not due to disease of the cells directly. Once started, fibrillation continues in the muscles after they have been disconnected from the anterior horn cells by nerve block.

SUMMARY

In this study the influence of sleep, nerve block, various stimuli and various drugs on fibrillation and tremor has been examined. The results lead to the conclusion that fibrillation and tremor are in different categories. Tremor is caused by rhythmic discharges from motor nerve cells whereas fibrillation is a phenomenon occurring primarily in muscles whose nerve supply is slowly degenerating. Impulses from the central nervous system and some physical stimuli directly applied to the muscle may increase fibrillation but not cause it.

525 East Sixty-Eighth Street.

8. Grund, George: Ueber die Entstehung des fibrillären Muskelzuchungen bei spinalen Amyotrophien, Deutsche Ztschr. f. Nervenh. **145**: 99-103, 1930.

SIMPLIFIED HORMONAL TREATMENT OF AMENORRHEA

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Amenorrhea may be a symptom of a general disease (diabetes, tuberculosis) but usually is of endocrine origin. As these conditions are often seen by the general practitioner, it is important for them to become acquainted with a simplified form of treatment. The tests for making clinical and hormone studies in these cases are frequently not at his disposal and therefore it is my aim in this paper to suggest a simplified method for producing bleeding in amenorrheic women.

The absence of menstrual bleeding is the cause of much concern to women. They suffer psychically and often an inferiority complex develops. The associated nervous and vasomotor disturbances frequently prevent these patients from attending their daily duties. As long as one is unable to put the motor of ovarian function into action, by means of gonadotropic stimulation therapy, one has to try at least to produce bleeding with normal substitution therapy. It is known that uterine bleeding may occur either from a proliferative (pseudomenstruation) or from a progestational mucous membrane (menstruation). To the women, it is of little significance from what anatomic structure of the uterine mucosa bleeding occurs. The two types of bleeding, from a proliferative and from a progestational endometrium, produce the same psychic and physical effects. Up until now it was generally thought that to produce bleeding the uterine mucosa had to be stimulated to proliferation by estrogenic hormone first and then the secretory phase had to be induced by progesterone. The doses required are from 30 to 40 mg. of estradiol benzoate and from 30 to 40 mg. of progesterone.[1] The treatment lasted twenty-five days. Daily injections of estrogen are not necessary, eight injections of 5 mg. each (estradiol benzoate) in the space of twenty days being sufficient, followed by daily injections of 5 mg. of progesterone for five days. In many cases a few days after the injections have been discontinued bleeding sets in. By this method, which is rather commonly used, the patient receives during one month of treatment at least thirteen injections. We find that this circumstance considerably accentuates the inferiority complex of which these women complain. For many years amenorrheic women have been treated in the manner described, i. e. they received parenterally from 30 to 40 mg. of estradiol benzoate a month, followed by from 30 to 40 mg. of progesterone.

The following observation[2] indicates that large quantities of estrogens are fully dispensable in the treatment of amenorrhea. If a normally menstruating woman receives in the early postmenstrual stage 10 mg. of progesterone[3] daily for five days, another bleeding appears in from sixty to seventy-two hours following the last injection. This bleeding occurs in the intermenstruum and has therefore been designated as "intracyclic bleeding." Biopsy shows that the bleeding originates from a thin mucous membrane, with only a

1. Kaufmann, C.: Zentralbl. f. Gynäk **56**: 2058 (Aug. 20) 1932; Klin. Wchnschr. **12**: 1557 (Oct. 7) 1933.
2. Zondek, Bernhard, and Rozin, Samuel: J. Obst. & Gynaec. Brit. Emp. **45**: 918 (Dec.) 1938; ibid. **46**: 736 (Aug.) 1939. Zondek, Bernhard, and Rozin, Samuel, and Vesell, Morton: Am. J. Obst. & Gynec. **40**: 391 (Sept.) 1940.
3. 1 mg. = 1 international unit.

few glands in the intermenstrual stage. This demonstrates the belief that a previous complete proliferation of the uterine mucosa by estrogens is necessary for the provocation of bleeding by progesterone to be erroneous.

These observations were utilized for the treatment of amenorrhea. It was surprising to find that a five day treatment with a total dose of 50 mg. of progesterone alone was sufficient to produce bleeding in amenorrheic women and that, therefore, the preparatory treatment with estrogens was quite superfluous. A further proof that the bleeding takes place from a very thin, hardly proliferated mucous membrane is shown by the fact that several successive bleedings can be induced in amenorrheic women if the progesterone treatment is repeated after an interval of two to three days. In this short interval only a minimal proliferation of the uterine mucosa can take place. This slight stimulus seems, however, to be indispensable. I have never succeeded in inducing bleeding with progesterone alone in women with primary amenorrhea or with castration amenorrhea.

Simplified Treatment of Amenorrhea

	Hormone Treatment				Uterine Bleeding	
Amenorrhea	Progesterone, Total Dose	Estradiol Benzoate, Total Dose	Duration of Treatment, Days	Number of Treated Cases	Number of Successful Cases	Percentage of Positive Results
Secondary	50 mg.	.....	5	20	18	90
	50 mg.	.....	2	7	6	85.7
	50 mg.	.....	1	4	1	25
	25 mg.	5 mg.	2	17	11	64.7
	25 mg.	5 mg.	1	8	4	50
Primary	50 mg.	2.5 mg.	5-8	6	6	100

The omission or, as will be seen, the limitation of the use of estrogen in the treatment of amenorrhea has the following advantages:

1. The detrimental effect on the gonadotropic function of the anterior pituitary is avoided, since progesterone, as far as is known, has no injurious effect on the anterior pituitary lobe.

2. The duration of treatment is shortened (from two to five days instead of twenty-five) which is psychically important to the woman. Since pregnen-in-on-ol [4] given orally has the same effect as progesterone given parenterally, the same results may thus be obtained in a simple five day treatment with a few tablets. It is possible with 300 mg. of pregnen-in-on-ol to obtain an intracyclic bleeding in normally menstruating women.[5] In secondary amenorrhea bleeding can also be produced with pregnen-in-on-ol. This dose is the minimal dose for a five day treatment.

3. Any possible carcinogenic influence is eliminated.

Our simplified method employed for the treatment of amenorrhea follows.

SECONDARY AMENORRHEA

(*a*) *Treatment for From Two to Five Days With Progesterone Alone.*—To the present time, 20 patients with secondary amenorrhea have been treated with progesterone alone. The patients were aged from 18 to 40 years and the amenorrhea had lasted from four months to seven years. A hypoplastic uterus was found in most instances. In 18 out of the 20 patients bleeding was obtained, i. e. 90 per cent of success. The patients regarded the bleeding in every respect as a regular menstruation, and the subjective symptoms have readily improved. The blood taken from the uterus did not coagulate.

Of the 18 successful cases, 9 could be followed up. In 4 of these cases no further bleeding took place, while in 5 cases further bleedings set in—however, not more than three times. One patient became pregnant. Thus it can be seen that a certain influence on the menstrual cycle is obtained. This mode of treatment does not, however, represent a stimulation therapy but mainly a substitutional therapy, since in half of the cases only a single bleeding followed.

The duration of treatment can be further reduced. Seven patients aged from 18 to 36 years whose amenorrhea had lasted from six months to six years had received 25 mg. of progesterone a day for two days. In 6 of the 7 patients a bleeding set in in from seventy-two to one hundred hours after the last injection. The treatment was successful in 85.7 per cent of the patients. If the 50 mg. of progesterone was given in one injection, no bleeding was obtained. A reduction in the total dose of progesterone is not possible, since bleeding does not take place with smaller doses. The minimal dose, therefore, is 50 mg. From these results one may deduce that the bleeding effect depends on two factors: (*a*) the dose of progesterone (50 mg. minimum) and (*b*) the duration of treatment (two days minimum).

(*b*) *Reduction of the Progesterone Dose by Addition of Estrogens.*—We made the interesting observation that the progesterone dose, minimum of 50 mg., may be reduced if the estrogen level in the body is increased. Seventeen women who had been amenorrheic for from six months to nine years were treated with 5 mg. of estradiol benzoate and 25 mg. of progesterone [6] on two consecutive days (2.5 mg. of estradiol benzoate and 12.5 mg. of progesterone daily). From eighty-four to one hundred and twelve hours after the last injection 11 patients reacted with uterine bleeding that lasted for from three to five days; 6 patients did not react at all. This led us to inquire into the probable cause of these failures. We found that the majority of nonreactors had amenorrhea of more than two years. It seems, therefore, that secondary amenorrhea of more than two years' duration should be treated with the full amount of 50 mg. of progesterone. The positive results (64.7 per cent) obtained will probably improve when the two day treatment is used only in cases of amenorrhea of less than two years' duration. When these patients were treated with estrogens and progesterone in one day instead of two days our results were very poor. Only 50 per cent of the patients reacted. We shall, therefore, continue with the two day treatment.

These results indicate that it is possible to reduce the duration of the treatment of secondary amenorrhea from four weeks to a very short time, as shown in the accompanying table. The method of choice is the "five day treatment" with 50 mg. of progesterone (10 per cent failure). The treatment can be further reduced to two days if 25 mg. of progesterone is given daily (14.3 per cent failure). If it is desirable to save progesterone, a total of 25 mg. of progesterone may be given

4. Pregnen-in-on-ol is the same as pregneninolone.

5. Zondek, Bernhard, and Rozin, Samuel: Lancet **1**: 504 (March 4) 1939.

6. The preparations used in this investigation were Dimenformon Benzoate and Progestin "Roche-Organon," put at our disposal by the Roche-Organon, Inc., Nutley, N. J. The two hormones were mixed in one syringe and simultaneously injected intragluteally.

in two days, but an additional dose of from 2.5 to 5 mg. of estradiol benzoate should be added simultaneously. This method should be restricted only to amenorrheas of less than two years' duration. The "one-shot method" is impracticable. Actually, I have gathered the impression that the treatment of secondary amenorrhea should be started with 50 mg. of progesterone; in the further course of the treatment this dosage may be reduced to 25 mg. of progesterone with the addition of from 2.5 to 5 mg. of estradiol benzoate.

PRIMARY AMENORRHEA AND CASTRATION AMENORRHEA

It has already been noted, the five day treatment with 50 mg. of progesterone gives good results in secondary amenorrhea but fails entirely in the treatment of primary amenorrhea. I have seen that in secondary amenorrhea the smallest stimulus for uterine proliferation is sufficient to produce bleeding. Since in primary amenorrhea no estrogenic hormone is produced, it seems reasonable to introduce small doses of this hormone in order to create conditions similar to those found in secondary amenorrhea. The results obtained have proved the correctness of this assumption.

The introduction of estrogens may precede the progesterone treatment or the two hormones may be given simultaneously in the same syringe. Three women aged from 30 to 39 years with primary amenorrhea received during four days from 0.5 to 1.25 mg. of estradiol benzoate a day, i. e. a total of from 2 to 5 mg. On the following five days 10 mg. of progesterone was given daily, a total of 50 mg. From three to four days after the last injection a bleeding of several days' duration took place in all 3 patients. Injections of 0.4 mg. of estradiol benzoate and 10 mg. of progesterone mixed in one syringe and given for five days in a woman aged 34 with primary amenorrhea led to bleeding on the ninth day after the onset of treatment. Two women aged 30, surgically castrated, received during five days a total of 5 mg. of estradiol benzoate and 50 mg. of progesterone simultaneously. Profuse bleedings occurred in both women on the eighth day. Their previous severe general complaints subsided. The duration of treatment (five days) should not be shortened. No bleeding took place in 6 patients with primary amenorrhea treated with estradiol benzoate and progesterone for one or two days.

COMMENT

The examination of the genital organs is not sufficient in determining the cause of amenorrhea; a general examination should be undertaken. An amenorrhea which is, for example, only a symptom in Cushing's syndrome involves different considerations than an amenorrhea occurring in a myxedematous patient. In cases associated with lowered basal metabolism the administration of thyroid is necessary, as has been stressed by R. T. Frank. Thyroid is still being insufficiently used in the treatment of amenorrhea. In cases in which the amenorrhea is caused by disorders of the sexual system, one should attempt to induce bleeding through sex hormones. There is no doubt that the production of bleeding not only relieves the women psychically but also greatly increases their physical well-being.

As has been demonstrated, it is erroneous to think that a progesterone-induced bleeding can take place only from a mucous membrane estrogenically prepared. In our simplified method the estrogenic hormone has a secondary role, the bleeding being brought about mainly by progesterone. Large doses of estrogens having an inhibitory effect on the anterior pituitary are avoided and the duration of treatment is reduced from four weeks to two to five days. The following are the methods of treatment:

1. In primary amenorrhea and in castration amenorrhea from 0.5 to 1 mg. of estradiol benzoate and 10 mg. of progesterone are mixed in one syringe and given intragluteally daily for five days. The total dose of this five day treatment will be from 2.5 to 5 mg. of estradiol benzoate and 50 mg. of progesterone. A shortening of the duration of treatment (i. e. less than five days) or the use of smaller amounts of progesterone is not possible. Since in primary amenorrhea the introduction of progesterone alone is insufficient, addition of estrogens is absolutely necessary.

2. In cases of secondary amenorrhea 10 mg. of progesterone is given intragluteally daily for five days, making a total of 50 mg. The duration of treatment may be shortened to two days by giving 25 mg. of progesterone daily. A further shortening of duration of treatment is undesirable. If progesterone is to be economized, addition of estrogens is necessary. We have found that it is best to inject in two days a total of 25 mg. of progesterone and from 2.5 to 5 mg. of estradiol benzoate. This is possible only in women with amenorrhea of less than two years' duration. Secondary amenorrhea of longer duration requires 50 mg. of progesterone.

It is interesting to note that the dose of progesterone is a decisive factor in producing bleeding. We found that 50 mg. is the optimal dose. A decrease of this dose reduces the percentage of good results considerably. The duration of treatment is also of importance. When 50 mg. is injected in secondary amenorrhea during two days, 85.7 per cent of the cases gave good results; but the same dose injected in one day reduced the success to 25 per cent. In primary amenorrhea 50 mg. of progesterone—besides the small amount of estrogens necessary—must be injected in five days. One hundred per cent of good results will then be obtained. When the duration of treatment was shortened to two days, no bleeding took place.

The interval between the last injection and the commencement of bleeding varies from seventy-two to one hundred and twenty hours.

SUMMARY

A new simplified method for the treatment of amenorrhea is as follows:

1. For secondary amenorrhea of more than two years' duration, a total of 50 mg. of progesterone distributed over from two to five days.

2. For secondary amenorrhea of less than two years' duration, the same dosage or a total of 25 mg. of progesterone with from 2.5 to 5 mg. of estradiol benzoate distributed over two days.

3. For primary amenorrhea and castration amenorrhea, a total of 50 mg. of progesterone with from 2.5 to 5 mg. of estradiol benzoate distributed over five days.

A further simplification will be possible by the oral administration of pregnen-in-on-ol instead of progesterone.

SYRINGOMYELIA

A CLINICAL EVALUATION

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Accepted concepts consider syringomyelia to be a tumor-like proliferation of glial cells with cavity formation. This involves the central portion of the spinal cord and brain stem. It is dependent on a developmental defect in the evolution of the neural tube permitting the arrest of embryonal cells.

There is some evidence to show that such a concept of syringomyelia is open to question.

Adult glial tissue constitutes the scar tissue of the nervous system. It is found wherever nervous tissue has been destroyed and healing has occurred, except in pyogenic infections. Ewing's work on Neoplastic Diseases [1] may be advisably quoted: "In an important group of cases, a pronounced central gliosis is associated with syringomyelia. Definite histological features of neoplastic growth are lacking. Some regard the process as a true neoplasm, while others consider it a form of inflammatory gliosis. There is no doubt that a pronounced gliosis is occasionally associated with cavity formation. On the other hand, syringomyelia may result from many processes not connected with tumor growth." The unique elongated gliosis with cavity formation does not conform with tumor growth elsewhere in the spinal cord. Here neoplastic tissue normally expands until it produces pressure symptoms in a localized area.

Syringomyelia notably affects the gray commissure, the ventral third of the lateral columns and the bases of the dorsal horns. This represents an area in the center of the cord from a vascular point of view. Ornsteen [2] has made a detailed study and gives an excellent description of the vascular supply to the substance of the cord. This central area receives blood from various radiating vessels. The most important of these are the vessels entering along the dorsal septum and the terminal branches of the ventral spinal arteries. These arteries are of small caliber. Some lie in a transverse plane, while others are longitudinal. Thus the vascular supply to this area of the cord is very meager. Any process which produces a thickening of the arterial walls or impairment of the circulation of the pial vessels on the surface of the cord may cause an ischemia of this area. The lymphatics similarly enter through dorsal routes and supply the central area. Both systems, therefore, offer direct portals of entry for infections and toxic substances to this vulnerable zone.

It is of interest to speculate on the selectivity of syringomyelia for the cervical, upper thoracic and lumbar portions of the cord. A definite relationship exists between the anatomic enlargements of the cord in these areas and the vascular structure. Ornsteen has shown that the caliber of the vessels is smaller in the lower cervical area. There is no appreciable increase in the number of vessels. Therefore one may assume that this area is more pregnable because the vascular supply is relatively less per unit area.

Tauber and Langworthy,[3] making india ink preparations of the spinal arteries of cats, demonstrated that the anterior and posterior spinal arteries, derived from the vertebral artery, were the sole source of blood as far caudally as the fifth cervical segment. Below this level the segmental arteries anastomose with the anterior spinal vessels and reinforce the supply of arterial blood. From their experiments they concluded that the circulation where these two systems unite was easily impaired by vascular disturbances and constituted an additional possible factor in the predominance of cavity formation at this site.

These investigators were successful in producing gliosis with cavity formation over several segments by ligation of the ventral half of the spinal cord of cats. Ligation of the dorsal half resulted in local necrosis in the area of the ligature. The difference may be due to the fact that the ventral ligation involves the circulation to those arteries supplying the greater part of the cord. Likewise they were able to produce central gliosis with cavitation by the injection of necrotizing substances such as 10 per cent dextrose or warm paraffin into the cord.

These experiments—partial ligation of the cord and the injection of necrotizing substances into the cord—illustrate two methods by which cavities may be produced with the formation of glial tissue. The resulting pathologic picture simulates the findings in syringomyelia.

Therefore it is only reasonable to assume that either one or both of these mechanisms may be present in syringomyelia. Certainly infection may cause the thrombosis of small arteries. Infection or toxins, carried to this vulnerable central area by arterial or lymphatic routes, may act as intramedullary necrotizing substances producing gliosis and cavitation.

In clinical neurology syringomyelia is generally regarded as a neoplasm, although many cases have been attributed to the interference of the vascular supply to the cord by a variety of agents. Holmes and Kennedy [4] in 1908 were among the first to report a case with autopsy material, a case of syringomyelia and syringobulbia secondary to syphilitic pachymeningitis. They expressed the opinion that the intraspinal disease was secondary to the meningitis and "due in some way to the compression of the cord or to the interference with its blood or lymph circulation." Similar cases have been recorded and the condition is recognized and accepted.

There is ample evidence from the study of such diseases as syphilis, poliomyelitis and heavy metal intoxications to conclude that infectious and toxic agents are capable of entering the central nervous system via perivascular, lymphatic and neural routes.

A review of a series of cases suggests that under certain conditions a focal area of infection may indirectly interfere with the vascular supply to the cord with the resultant syrinx and gliosis.

From the Neurological Service and Second (Cornell) Medical Division, Bellevue Hospital, and the Department of Medicine, Cornell University Medical College.

1. Ewing, James: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, 1934.

2. Ornsteen, A. M.: Thrombosis of the Anterior Spinal Artery, Am. J. M. Sc. **181:** 654 (May) 1931.

3. Tauber, E. X., and Langworthy, O. R.: A Study of Syringomyelia and the Formation of Cavities in the Spinal Cord, J. Nerv. & Ment. Dis. **81:** 245 (March) 1935.

4. Holmes, G., and Kennedy, F.: Two Anomalous Cases of Syringomyelia, Brain **31:** 494, 1908.

During the ten year period 1928-1938, 42 cases were diagnosed as syringomyelia in the wards of Bellevue Hospital. Of this group 33 have been selected for study. The remainder were excluded for various reasons; some had not been studied in the neurologic service; in others, controversy of opinion existed with regard to diagnosis. Only those cases were considered in which a complete neurologic examination had been made and the majority of observers agreed as to the diagnosis. Cases were rejected when the diagnosis of intramedullary tumor was not definitely excluded.

In general, the historical facts and the clinical and laboratory data obtained in the series conformed with the accepted picture of the disease. Some of the data merit special consideration. The age of onset ranged from 16 to 51 years. The greatest incidence was in the second and third decades. Seventeen of the cases gave a history of some unusual infection within one year prior to the onset of symptoms. Three cases were related to heavy metal intoxication. Six cases were considered traumatic. Of the remaining 7 cases, no definite data were recorded in the history which would point to any specific etiologic agent. Of these, 1 case (reported in detail) came to operation and showed evidence of an old infectious process. It is of interest that all the cases in which trauma with secondary hemorrhage was thought to play a role in the production of the syringomyelia occurred after the age of 40. All cases in which infection may have been a factor occurred before that age.

Seventeen cases in which syringomyelia may have been caused directly or indirectly by infection will now be considered. In 13 of the 17 cases the onset of signs and symptoms occurred in the extremity nearest the infected area. This is a striking fact. It is acknowledged that the relationship is purely presumptive; on the other hand, to deny that such a relationship exists is equally presumptive.

REPORT OF CASES

Five illustrative cases are now presented:

CASE 1.—J. H., a man aged 23, a messenger, had had bouts of productive cough and night sweats of many years' duration. Seven years before admission to the neurologic service he began to complain of numbness and tingling of the fingers of the left hand. Gradually the hand became weak. The process spread to involve the arm and shoulder girdle to such a degree that he was unable to abduct his arm. An atrophy of the intrinsic muscles of the hand occurred and resulted in contractures of the fingers. A tenotomy was performed three years after the onset in an attempt to correct the deformity. Three years before admission a similar involvement of the right arm occurred to a lesser degree. The lower extremities remained uninvolved.

The patient was thin and appeared chronically ill. Examination of the lungs revealed dulness and crepitant rales at both apexes, more extensive on the left, where there was evidence of cavitation. Chest signs were confirmed by roentgenograms.

Neurologic examination revealed a Horner's syndrome on the left. Extraocular movements were normal except for a coarse nystagmus on lateral gaze. There was atrophy of the muscles of the shoulder girdle and the upper extremities, more severe on the left side. Deep reflexes were absent in the upper extremities, present and equal in the lower. There was no evidence of pyramidal tract involvement. Sensation of pain and temperature was impaired from the third cervical to the third dorsal. Position and vibration sense was impaired in the upper and lower extremities. Trophic changes in the fingernails of the left hand were present.

Laboratory data revealed no significant changes; the blood and the urine were normal. The blood Wassermann reaction was negative. The spinal fluid was of normal pressure and gave no evidence of block, with normal cell count and total protein. The Wassermann and colloidal gold curve were negative.

This was a case of syringomyelia of the upper extremities with the onset and greater involvement on the left side in a patient with bilateral chronic pulmonary tuberculosis with the oldest and most extensive changes at the left apex.

CASE 2.—F. R., a man aged 27, an athletic instructor, had had severe follicular tonsillitis for many years. In 1926, five years before the initial examination, a tonsillectomy was performed. In the same year he noted the onset of a dull aching pain over the left clavicle, which radiated over the left shoulder. Shortly afterward the right shoulder girdle had similar involvement, which extended to the anterior surface of the right side of the chest. Approximately two years later he became aware of a weakness and wasting of the muscles of the upper extremities. One year later the right side of the chest became numb and the right leg became weak. A few months before entering the hospital, the patient noted numbness and shooting pains involving the right side of the face.

General physical examination revealed that the tonsils were absent; there was a moderate enlargement of the cervical lymph nodes. The remainder of the examination was noncontributory.

The neurologic examination showed atrophy and fibrillation of the muscles of the shoulder girdle and the upper extremities. In the lower extremities, signs of bilateral pyramidal tract involvement was demonstrated. Temperature and pain sen-

Seventeen Cases in Which Syringomyelia May Have Been Caused by Infection

Case	Type and Site of Infection	Site of Onset of Initial Symptoms and Signs of Syringomyelia
1. J. H.	Chronic pulmonary tuberculosis of left apex	Numbness of the fingers of left hand
2. A. G.	Chronic pyelitis	Weakness of left leg
3. L. L.	Severe sore throats; tonsillectomy	Weakness of left arm
4. R. G.	Twenty-seven felons in two years	Pain in shoulders
5. H. C.	Severe sore throats; tonsillitis	Weakness of right arm
6. F. R.	Severe tonsillitis; pyelitis	Pain over left clavicle
7. D. H.	Encephalitis	Onset in legs; weakness
8. M. L.	Tonsillectomy; right mastoidectomy	Numbness in right hand
9. W. L.	Frequent colds and sore throat	Weakness and numbness of left hand
10. A. F.	Syphilis	Pain in the right leg
11. J. C.	Syphilis	Weakness of the left foot
12. J. G.	Spondylitis, lumbar	Pain in right thigh
13. M. M.	Spinal syphilis	Numbness in right hand
14. H. C.	Frequent severe colds	Numbness in both thumbs
15. A. G.	Tuberculosis of right shoulder joint	Numbness of the right hand
16. T. P.	Injury to cervical vertebrae; infection of finger on right hand	Weakness of right hand
17. W. R.	Right acute purulent otitis media; spontaneous discharge of pus behind right ear	Weakness of right arm

Only those infections which were present within a year prior to the onset of the disease are included.

sation was lost from the third cervical to the seventh dorsal in the upper portion of the cord and in the lower from the second lumbar to the first sacral vertebra.

Laboratory examination showed no abnormalities; the blood and the urine were normal. The spinal fluid was under normal pressure with no evidence of block. The Wassermann and colloidal gold tests were negative.

This was a case of syringomyelia which had its onset in the shoulder girdle of a patient with chronic follicular tonsillitis. The onset of symptoms occurred in the same year in which a tonsillectomy was performed.

CASE 3.—W. L., a man aged 32, a clerk, had an appendectomy at 13, herniorrhaphy at 15 and repair of a rectal fistula at 19. The present illness began three years before his admission to Bellevue at the age of 28, at which time he had a generalized infection which was diagnosed as influenza. Shortly afterward he began to experience tingling sensations in the fingers of both hands, at the same time noticed that he had difficulty in flexing his feet, and later observed that his right foot slapped the ground as he walked. Several months after the onset he discovered that the right leg was smaller than the left. In April 1931 he first noted weakness in the right arm. He believed that the right leg had improved and was stronger. In May 1932, following a severe infection of the upper respiratory tract, the right arm became weaker and weakness of the right leg developed. In January 1932, following another severe respiratory infection, he observed increasing weakness in both arms and legs. He began to have difficulty in swallowing and complained that his tongue felt heavy. Neurologic examination revealed muscular atrophy with fibrillary twitching of the right side of the tongue, some bilateral atrophy of both sternocleidomastoid muscles and difficulty in swallowing. There was weakness of the right arm and leg with moderate atrophy. The deep reflexes were overactive on the right side, and there was a positive Babinski and Hoffmann sign on the right. A segmental sensory defect to pain and temperature was found in the presence of normal tactile, vibration sense from the second cervical to the eleventh dorsal vertebra on the right side. The laboratory data were normal. The spinal fluid was normal. The blood and spinal fluid Wassermann reactions were negative.

A diagnosis of syringomyelia was made. Each exacerbation of symptoms and signs of syringomyelia was preceded by a severe upper respiratory infection.

CASE 4.—W. R., a man aged 49, a waiter, had had a severe middle ear infection eight years before. Pus drained spontaneously from behind the right ear. A year later he began to have pain in the upper midscapular region with partial loss of motor power in the right arm and numbness in the right arm and face. Sensation returned in the face after a period of three years. After a year and a half before the present examination, the pain began to radiate to both shoulders and extend down both arms; there was a well defined weakness of the right arm with a gradual contracture of the right hand. In the course of the next six months the patient experienced paresthesias in the fingertips of the left hand and began to have gradually increasing weakness in both legs, more pronounced on the right.

Neurologic examination showed a right Horner's syndrome, atrophy of the right side of the tongue, deviation of the tongue to the right and atrophy of the small muscles of the right hand, right upper arm and shoulder girdle. There was a spastic paresis of the right leg. The deep reflexes were absent in the upper extremities bilaterally and were present in the lower but hyperactive on the right. A bilateral Babinski reflex was extensor in character. There was a loss of pain and temperature sensation on the right between the second and eighth cervical vertebrae and a loss of posterior column sensation in the right hand. Sensory examination was otherwise normal.

Laboratory data were normal. The blood and spinal fluid Wassermann reactions were negative.

A diagnosis was made of syringomyelia and syringobulbia, severe right middle ear and mastoid infection prior to onset of symptoms in the right shoulder and arm.

CASE 5.—T. C., a man aged 44, Italian, a laborer, had no history of any infections. Illness began about four years before the present examination, with wasting of the small muscles of the hands, shaking of the legs and inability to walk because of spasticity of the legs.

Neurologic examination revealed a spastic paraplegia and weakness of both legs. There was atrophy of the musculature of the arms, including the intrinsic muscles of the hands. The reflexes were absent in the upper extremities and hyperactive in the lower, with bilateral extensor plantar response. Temperature and pain sensation were impaired below the sixth cervical vertebra bilaterally. Vibration sense was diminished on the right; tactile sense was normal throughout.

Laboratory data were normal. The blood and spinal fluid Wassermann reactions were negative.

An exploratory laminectomy was performed in the upper thoracic and lower cervical area. The appearance of the cord at operation revealed that the arteries were engorged and tortuous and led to the following postoperative diagnosis being made: "intrinsic inflammatory cord disease with tortuous engorged vessels and possible internal gliosis."

COMMENT

Thirty-three cases of syringomyelia have been considered. These represent all the cases of syringomyelia in Bellevue Hospital from 1928 to 1938 in which a complete neurologic examination was performed and a definite diagnosis made. In 17 cases it is found that an infection was present within a year of the onset of signs and symptoms of the disease. This infection was unusual in character, severity or duration. In 14 cases the onset of signs and symptoms of syringomyelia involved nerve segments in close proximity to and on the same side as the focus of infection.

It is contended that syringomyelia is not necessarily a neoplasm; that syringomyelia may be caused by infection or toxins through their ability to produce impairment of the circulation of the cord or necrotizing action within the cord.

The review of pathologic and experimental data and the analysis of 13 cases of syringomyelia showing the presence of infection and the relation between the onset of signs and symptoms and the infected area adequately supports this contention.

SUMMARY

1. Experimental work shows that the central portion of the spinal cord, because of the structure of the vascular and lymphatic supply, is vulnerable to infectious agents.

2. Gliosis with cavity formation has been produced experimentally by the ligation of parts of the spinal cord and the injection of necrotizing substances such as 10 per cent dextrose or warm paraffin.

3. Clinical evidence of the disease was recorded of 17 cases of syringomyelia, which may have been related to infection.

4. There is an apparent relationship between the infectious site and the site of the onset of syringomyelia.

2 Sutton Place, South.

Clinical Notes, Suggestions and New Instruments

HYPERTENSION CAUSED BY UNILATERAL RENAL COMPRESSION

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Renal compression has not been considered a cause of hypertension until recently. Page [1] reported the occurrence of hypertension in experimental animals in which a kidney had been enclosed in cellophane. The cellophane caused a tissue reaction around the kidney which resulted in a fibrous hull. This fibrous hull completely enclosed and compressed the renal parenchyma and caused hypertension in dogs, cats and rabbits.

No case has been reported in the literature in which renal compression of an analogous nature has caused hypertension in man. The following case resembles Page's experimental production of hypertension in animals by renal compression.

Fig. 1.—Bisected cyst and kidney, revealing the intramural position of the kidney.

REPORT OF CASE

History.—D. P., a student aged 18, was examined by a school physician and found to have a blood pressure of 154 mm. of mercury systolic and 102 mm. of mercury diastolic. He had no complaints. On physical examination a large, fluctuant, nontender movable mass could be felt in the right renal region. The patient was unaware of this mass. His mother, when told about the mass, remembered an injury which the boy had sustained at the age of 6 years. He had been struck over the right kidney with a roller skate hurled by a playmate. There was discoloration of the skin over the region of the right kidney. The boy was put to bed for a day. The mother observed no ill effects from this injury. There was no history of urinary symptoms at any time.

Further physical examination revealed an accentuation of the aortic second sound. Vascular changes were not observable in the eye.

The urine was normal. Blood chemistry and morphology were normal.

When an intravenous urogram was made the right kidney excreted the opaque material in normal time. The right renal pelvis was displaced medially and could not be seen distinctly. The left kidney was normal. A retrograde pyelogram of the right kidney revealed that the kidney had been displaced by compression at its lower and lateral borders. A large area of increased density lateral and below the kidney measuring 14 cm. in diameter appeared to cause the displacement of the kidney. This area of increased density, from its contour and position, suggested a cyst of the kidney.

Operation.—Under ethylene anesthesia a right lumbar incision was made. A large fluctuant mass was exposed. This mass extended from the ninth rib to the crest of the ilium. The mass extended beyond the midline medially. Incision of the cyst released about 800 cc. of chocolate colored fluid mixed with old fibrin. After evacuation of the cyst, a flattened kidney with hard bonelike edges could be felt in the wall of the cyst. Because of the possible association of a malignant growth and hemorrhagic cysts, the kidney was removed.

PATHOLOGY

Gross Appearance (figure 1).—The specimen consisted of a large solitary cyst 14 cm. in the transverse diameter, 18 cm. in the longitudinal diameter and 33 cm. in circumference. The right kidney was enclosed within the medial wall of the cyst. The specimen weighed 338 Gm. after approximately 800 cc. of thin, chocolate colored fluid had been removed. Fatty areolar connective tissue surrounded the renal vein, two renal arteries and the proximal attached 3 cm. of ureter. A capsula adiposa was also adherent to the external surface of the cyst. The cyst was about one third filled with chocolate colored, turbid fluid mixed with dark brown-red crumbs. The firm collagenous wall of the cyst varied from 3 to 4 mm. but increased to 5 mm. over the convex surface of the medial surfaces of the kidney and renal pelvis. The renal capsule was fused with the cyst wall. The kidney was 11.5 cm. long, 6.5 cm. in the transverse diameter and 3 cm. thick. The kidney occupied an intramural position in the medial wall of the cyst. The internal sheath of the cyst covering the convex or lateral surface of the kidney was transformed to irregular cartilaginoid and partly calcified plaques varying from 3 to 4 cm. in diameter.

Two renal arteries, from 3 to 4 mm. in diameter, entered the kidney. The inferior artery entered the cyst wall covering the hilus of the kidney ventral to the renal pelvis, while the superior artery entered dorsal to the pelvis. The vessels had thick sclerotic walls and narrow lumens.

The external surface, when separated from the cyst, was smooth. Sectioned surfaces revealed a distinct corticomedullary differentiation. The pale gray cortex was 5 mm. thick. The linear striations were not prominent. The medulla was 12 mm. thick. The pyramids were pale red. There were a few small irregular submucosal hemorrhages in the pelvis. The lining of the major calices, renal pelvis and proximal ureter was smooth.

Microscopic Appearance (fig. 2).—The lateral wall of this cyst was formed by a thickened layer of partially hyalinized collagen-connective tissue. No internal identifying membrane was seen. A few areas of bone formation were present. These have a typical pink matrix, Haversian canals, nutrient vessels and a delicate reticulated marrow structure devoid of hemopoietic elements.

Sections taken through the midportion of the convex surface of the kidney were covered by the wall of the cyst. The delicate fibrous capsule of the kidney was intimately fused with the cyst wall. The kidney capsule was identified by delicate strands of collagen-connective tissue, while the wall of the cyst was similar to that already described. The kidney cortex displayed slight subcapsular interstitial fibrosis and round cell infiltration. The precapillary arterioles in this region were thickened. The arcuate and interlobular arteries in this region exhibited no decided change. Neither did the kidney parenchyma. Sections from the poles of the kidney including the ensheathing wall of the cyst and renal pelvis displayed the following:

The cyst wall, formed by partially hyalinized collagen-connective tissue in which were focal infiltrations of lymphocytes,

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1. Page, I. H.: The Production of Persistent Arterial Hypertension by Cellophane Perinephritis, J. A. M. A. **113:** 2046-2049 (Dec. 2) 1939.

was intimately adherent to the renal capsule. The latter was more compact and thickened than the capsule described over the convex surface. The subcapsular parenchymal changes in this region were greater than they were on the convex surface of the kidney. Several of the glomeruli were replaced by connective tissue. There was some atrophy of the appertaining tubules, associated with interstitial fibrosis and round cell infiltration. The ventral and dorsal renal arteries entered the kidney through the wall of the cyst and capsule. They had thick walls, formed partly by hyperplasia of the media and subendothelial proliferation of fibroblasts to form thickened intima. The fibroblasts of the thickened intima were growing perpendicular to the media. One such vessel had a slight bluish myxomatous degeneration of the stroma. No evidence of fatty degeneration or calcification was seen. One of these vessels was almost completely occluded by reduplication of the elastic lamina and hyperplasia of the media. The major branches of the renal vein were thicker than normal, and in their walls

Fig. 2.—Hyperplastic sclerosis and stenosis of small branch of the anomalous renal artery.

were small arteries which had undergone the same hyperplastic thickening as that described. The mucosa of the major calices and renal pelvis was intact. The edematous subepithelial zone contained a few small hemorrhages. The proximal ureter was normal.

The diagnosis was right solitary cyst with intramural kidney, diffuse hyperplastic sclerosis of the renal arteries and secondary heteroplastic ossification of the cyst wall.

The day after the operation the blood pressure was 118 systolic and 78 diastolic; two weeks after the operation the blood pressure was 104 systolic and 62 diastolic, six months later the blood pressure was 110 systolic and 74 diastolic, and ten months later it was 114 systolic and 74 diastolic.

COMMENT

This boy sustained an injury at the age of 6 years which resulted in the formation of a hemorrhagic cyst, resulting in the envelopment of the kidney parenchyma in the walls of the cyst. The walls of the cyst thickened and appeared to have exerted compression on the kidney. The sclerosis and thickening of the blood vessels caused by this compression resulted in hypertension. Removal of the kidney brought the blood pressure to normal.

There were three noteworthy features in this case. The factor of age was eliminated as a cause of hypertension. Evidence of infection which might have caused renal damage was not found. The blood pressure promptly returned to normal after nephrectomy. The pathologic and clinical observations closely simulate the experimental hypertension produced in animals by cellophane perinephritis.

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Special Articles

SURGICAL EXPERIENCE AT PEARL HARBOR

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The attack on Pearl Harbor began about 7:50 a. m. on Sunday, Dec. 7, 1941, and shortly thereafter with several civilian surgeons from Honolulu I began operating at a large military hospital. The following is a brief account of some of the major surgical situations encountered in the period between December 7 and January 2:

NATURE OF CASUALTIES

The casualties were numerous, varied and severe. The majority were the result of bombing or machine gun attack. The embedded foreign bodies were of variable size and depth. Several casualties were of the most unusual type; such, for example, as an arteriovenous aneurysm at the carotid bifurcation. Also a machine gun bullet lodged in the spinal canal at the second lumbar level. The majority of the casualties consisted of multiple lacerated wounds and compound comminuted fractures. Intrathoracic cases did extremely well; but the intra-abdominal group furnished the largest mortality. There were relatively few intracranial cases, but peripheral nerve injuries were numerous. Loss of limbs, initial or from operation, resulted in only a few postoperative fatalities. Shock and hemorrhage were common, but these were surprisingly well combated by transfusion of blood or liquid plasma. Burns were very rare in our formation; elsewhere they were the major group but fortunately most of them were of the first degree and second degree variety.

PROCEDURE

On arrival, the wounded were triaged (sorted) and given preliminary sedation of ½ grain (0.03 Gm.) morphine when indicated. Previously all the wounded had received the standard tetanus toxoid inoculations on entry into the service. However, when any extensively muscled area was involved or in regions grossly contaminated, an additional 1 cc. of tetanus toxoid was given. Shock was treated by transfusion of whole blood or liquid plasma or by infusion of saline-dextrose solution.

Anesthesia was usually by gas-oxygen-ether sequence, the induction often preceded by intravenous evipal or pentothal sodium. The last named agents were often used throughout and in some cases were administered through a puncture into the transfusion or infusion tubing close to the bend of the elbow. Very few spinal, rectal or local anesthesia procedures were undertaken.

Authorized for publication by the Office of the Surgeon General, U. S. Army.

I had arrived in Honolulu on December 3 at the invitation of the Honolulu Medical Society to give a course of lectures on "Traumatic Surgery." By a strange coincidence the second lecture was entitled "Treatment of Wounds, Civil and Military," and this was given on Friday night, December 5, approximately thirty-six hours before the attack. An audience of about three hundred attended, and a large proportion represented the Army and Navy medical personnel. At this lecture, virtually a rehearsal, stress was placed on early adequate cleansing of wounds by soap and water, followed by débridement to fulfil the three criteria of (1) obtaining normal color, (2) bleeding and (3) muscle contraction—all these to be attained by nonsacrificial exsection of any involved tissues. Thereafter absolute hemostasis was advised, to be followed by placing in the wound an adequate amount of a sulfonamide drug, either sulfanilamide or sulfathiazole. No wounds were to be sutured, but instead left wide open or to have nonabsorbable interrupted sutures placed, but not tied until the third day if all went well (primosecondary suture). Heavy plain gauze dressings were to be applied, and splintage added if joints were contiguous. As part of the after-care, 15 grains (1 Gm.) of a sulfonamide drug was to be given every four hours for three days together with needed sedation. No redressings were to be applied for forty-eight to seventy-two hours unless indicated. These were the recommendations and they were based on experience in World War I and also in civil practice. No one then thought that these principles of treatment were so soon to be put to a large scale test in a proving ground only a short distance from the lecture platform.

When we began work on the morning of the attack there was the inevitable confusion caused by the influx of a large number of casualties, but very soon eight operating teams were on duty and most of us operated continuously for eleven hours. We were relieved by another group, and by this time a six hour shift was started; later this became a four hour tour. Most operations were performed by the civilian surgeons at the onset, as the regular hospital personnel were engaged in the essentially important triage shock, ward work and treating the walking wounded so that they might be discharged to duty. I was restored to temporary active duty in the Army Medical Corps as Colonel, Surgical Consultant, soon after the attack began.

Fractures were mainly of the extremities, often multiple and practically all grossly compounded, with retained metallic foreign bodies and débris. Débridement was done as for any wound, and splintage was in a Thomas arm or leg splint, with or without skeletal traction by transosseous wire. No plates were inserted; a few fractures were encircled with stainless steel wire. Plaster of paris casings were occasionally used when the compounding was not severe; otherwise encirclement was purposely not advised.

In the intrathoracic group, after débridement, tight closure was employed around an indwelling tube, which was connected to under water drainage. This gave us excellent results and we had no cases of empyema despite the necessity for later using aspiration in some cases to provide better decompression for hemothorax. Indwelling foreign bodies were not searched for unless accessible. For subsequent search for foreign bodies within the chest, one of the surgical personnel has been advised by me to perfect himself in the technic used by the French surgeon Petit de la Villon in the last war. This consists of a stab wound in the intercostal space, through which a long thin clamp is introduced, and then this grasps and removes the foreign body under the guidance of the fluoroscopic screen. It is a very dramatic and successful procedure.

The intra-abdominal group were treated by débridement of the original wound or wounds, and then these were packed with a sulfonamide derivative and left unsutured. A separate median laparotomy incision followed, and this was sutured later by the ordinary laparotomy technic. Intestinal perforations were sutured with silk, and no resections were done unless the damage was extreme. All sutured areas were coated with a sulfonamide drug and the same drug was placed within the abdomen. Our mortality in this group was high. In 1 fatal case of my own there were twenty-one perforations of the jejunum and ileum following a machine bullet wound penetrating the left lower abdominal quadrant and lodging under the liver.

The intraspinal group did well and we had 2 successful cases in which a machine gun bullet had lodged within the spinal canal. In 1 of these I would have failed had it not been for the aid afforded by the "locator." This is an electromagnetic induction apparatus about the size of a portable radio and it functions after the manner of a detector of buried metals. It was developed for me by a very clever technician of the New York City Transit System, and I gave it a successful trial at the Reconstruction Hospital Unit of the New York Post-Graduate Hospital just before leaving for Honolulu. This initial demonstration was in the case of a police officer who had been in the bombing incident at the New York World's Fair in July 1939. At this first test of the locator I was able to locate and remove several small metallic fragments from the region of the ankle, and purposely the x-ray films were not used as additional guides. This apparatus is highly sensitive for fragments of iron, steel, brass and copper, as well as for silver and aluminum, and less so for lead. It indicates the foreign body on the surface by a dial and also registers the subsurface depth almost equally well. The wandlike finder or probe can be sterilized and introduced into the wound if necessary. It was by this last named application that I found the aforementioned intraspinal bullet.

On two successive days during a calm period we gave the locator a severe test in our hospital group, and it proved helpful in 22 cases in which operations were performed by the chief of the surgical service and his assistants. The original apparatus is in Honolulu, but another even more responsive has been tested, and soon the device will be available commercially.

The intracerebral group numbered relatively few, and, as is the rule, survival was rare. Our procedure was débridement of soft tissues and bone, gentle intracranial irrigation and limited search for the foreign body. The dura was sutured, with partial closure of the overlying tissues followed by drainage to the bone level.

Amputations were of the "chop" or "guillotine" variety. In certain cases a modification seems permissible in this technic and it will be subsequently described elsewhere. At the end of the "third period" we attached traction straps to the amputation stump and made some patients ambulatory by applying a plaster spica. Into this we fastened the looped wire from a coat hanger and thereto attached the adhesive traction straps. Instead of using the wire transfixion of the olecranon, in one fractured lower humerus we inserted a screw eye into the base of the olecranon and to this attached our traction. It is simple and

efficient, and local anesthesia suffices. Later I intend trying it for leg fractures, inserting the screw eye through the sole into the os calcis.

RESULTS

We had several cases of gas gangrene, and most of these were confirmed by the laboratory, but none showed true Clostridium perfringens (Bacillus welchi), although many other anaerobes could be identified. A separate gas gangrene ward was established. Under the combined use of (1) secondary débridement, (2) sulfanilamide in the wound and by mouth and (3) x-ray exposures, all patients recovered without amputation. In every case of gas gangrene the wound had been too tightly sutured despite advice to the contrary.

Purulent exudate was practically absent, so much so that it became a subject of universal comment.

We had no cases of tetanus, local or general. The state of well being of the wounded was exceptional after the first few days. Those in need of stimulation were given a transfusion, and we tried to get many of them outdoors, especially the gas gangrene group, so that the wounds might benefit from sunlight exposure in the balmy air of this wonderful climate (average temperature at this season 65-70 F.).

On January 3 in a San Francisco hospital I visited a large group of wounded we had evacuated on Christmas day, and they were all doing exceedingly well. Their condition elicited a special report to headquarters. Hence the follow-up is sufficiently prolonged to permit evaluation of the end-results.

COMMENT

1. A very large number of seriously wounded arrived at a military hospital within a period of five hours.
2. The postoperative mortality was 3.8 per cent.
3. Most of the fatalities were in the intra-abdominal group and among those depleted by shock and hemorrhage.
4. No deaths resulted from gas gangrene.
5. Purulent discharge was almost absent.
6. The results were better than I had ever seen during nineteen months in France when serving with the French, Belgian and American medical formations.

The outcome was dependent on:

(*a*) Early receipt of the wounded—within the "golden period" of six hours.

(*b*) Preliminary shock treatment.

(*c*) Adequate débridement with no primary suturing.

(*d*) Use of sulfonamide drugs in the wound and by mouth.

(*e*) Adequate after-care.

Other factors which aided were:

(*a*) Absence of puttees; the incidence of driven-in dirty apparel was thereby lessened.

(*b*) Climatic conditions.

(*c*) Early hour of the attack; Sunday morning, and the men were clean and were not war worn.

(*d*) Few flies.

Our greatest defect was inability to give better preoperative shock treatment to a larger number of the seriously wounded.

The outstanding features in this initial outbreak of World War II were the morale of the wounded, the unusual skill of the surgeons and the devoted service of the nursing and other hospital personnel.

It is a duty and a proud privilege to pay tribute to those who served, and no directing surgeon ever had better cooperation.

115 East Sixty-Fourth Street.

DIPHTHERIA MORTALITY IN LARGE CITIES OF THE UNITED STATES IN 1940

EIGHTEENTH ANNUAL REPORT

The data for this review have been obtained from the local health officers through the means outlined in the report on typhoid deaths.[1] There was requested from each health department a statement of deaths from diphtheria both among residents and among nonresidents for each of the last eleven years, 1930 to 1940 inclusive. The death rates have been corrected on the basis of the 1940 census, provisional estimates for intercensual years having been furnished by the Bureau of the Census. No attempt has been made to correct the number of deaths reported prior to 1935.

Special attention is directed to the use of symbols to indicate those cities in which either (1) all diphtheria deaths were stated to be in nonresidents or (2) one third or more of such deaths were stated to be in nonresidents. Table 11 lists the cities with no death in 1940, table 13 the cities which would be included in such an honor list unless burdened by deaths among nonresidents.

The fourteen New England cities (table 1) report a continued downward trend in the death rate for the group as a whole (0.50 in 1939, 0.23 in 1940); but, in spite of this striking reduction of more than 50 per cent, they have not been able to overhaul the cities of the Middle Atlantic states, which continue to hold first place (table 16). Ten cities (there were but seven in 1939) report no death from diphtheria in 1940 (Bridgeport, Cambridge, Lowell, Lynn, New Bedford, New Haven, Somerville, Springfield, Waterbury, Worcester). It is stated that the two deaths reported in Providence occurred among nonresidents, there having been but one death among residents in this city since 1935. Lynn, alone among the ninety-three cities, records no typhoid and no diphtheria death during the

TABLE 1.—*Death Rates of Fourteen Cities in New England States from Diphtheria (Including Croup) per Hundred Thousand of Population*

	1940	1939	1935-1939	1930-1934	1925-1929	1920-1924	1915-1919	1910-1914	1905-1909	1900-1904	1895-1899	1890-1894
Springfield	0.0	0.0	0.3*	2.1	10.3	15.4	24.9	19.1	31.3	29.6	51.3	68.2
New Haven	0.0	0.0	0.4*	0.7†	1.6	7.1	14.2	14.9	22.7	15.6	54.8	74.5
Lynn	0.0	0.0	0.4	4.7	13.5	17.0	17.8	17.2	21.7	38.0	44.0	49.0
New Bedford	0.0	0.0	0.4	5.0	10.9	16.5	17.0	20.9	22.6	25.1	53.6	30.0
Somerville	0.0	0.0	0.4	9.3	5.7	19.7	20.2	21.4	21.5	40.5	57.8	37.4
Waterbury	0.0	0.0	1.4	2.4	2.6	17.9	23.0	29.6	....	....	....	....
Lowell	0.0	0.0	2.8	9.4	10.6	16.7	23.5	20.6	31.0	59.3	44.3	36.4
Cambridge	0.0	0.8	0.3	1.2	3.2	8.9	12.9	23.8	25.3	46.7	71.9	58.0
Worcester	0.0	1.0*	0.7†	3.3†	8.6	15.5	14.1	21.3	32.2	16.5	50.3	47.8
Bridgeport	0.0	1.3	0.8	1.2	11.8	19.6	23.4	23.3	26.8	34.2	63.9	79.3
Boston	0.3†	0.4†	0.7†	3.2†	8.3	20.2	26.3	20.0	26.2	53.7	83.9	112.2
Hartford	0.6	0.6*	1.9†	1.1†	5.3	11.9	13.8	25.3	28.1	38.8	47.8	120.9
Providence	0.8*	0.4	0.6†	5.1	9.5	15.8	29.3	26.8	30.7	41.2	53.5	55.3
Fall River	0.9	2.6	2.4	3.6	12.0	25.5	23.6	24.0	34.4	50.1	43.8	46.9

* All diphtheria deaths were stated to be in nonresidents.

† One third or more of the reported diphtheria deaths were stated to be in nonresidents.

The preceding articles were published in THE JOURNAL Sept. 20, 1924, p. 918; April 25, 1925, p. 1269; April 3, 1926, p. 1005; April 30, 1927, p. 1396; May 19, 1928, p. 1621; May 25, 1929, p. 1759; June 7, 1930, p. 1838; May 23, 1931, p. 1768; May 7, 1932, p. 1644; May 20, 1933, p. 1595; May 26, 1934, p. 1758; June 15, 1935, p. 2182; June 13, 1936, p. 2060; June 26, 1937, p. 2200; Aug. 6, 1938, p. 524; May 20, 1939, p. 2043, and May 11, 1940, p. 1875.

1. Typhoid in the Large Cities of the United States in 1940, J. A. M. A. **118:** 222 (Jan. 17) 1942.

past four years (table 12). New Bedford reports no typhoid death for four years, no diphtheria death for three years. Lowell has completed a period of three years with no death from either cause. Springfield has been without a death from diphtheria for four years, without a typhoid death for two years. Furthermore, it is stated that no diphtheria death has occurred in a resident of Springfield during the past eight years. New Haven reports no diphtheria death for three years. Boston records two deaths in 1940, one among residents. Of eighteen deaths that occurred in this city during the five years 1936-1940, eight were among nonresidents. For these same five years, Hartford reports ten deaths with but two among residents. One of these resident deaths occurred in 1940. The health officer states that about 82 per cent of entering school children have already received their diphtheria protection treatments.

The eighteen cities in the Middle Atlantic states (table 2) continue to hold first place, with a group rate of 0.20 (it was 0.37 in 1939). The new rate represents a new all time low, but the cities of the New England group are not far behind. In 1939 there were forty-nine deaths and in 1940 but twenty-six. Twelve cities (there were nine in 1939) report no diphtheria death in 1940. Eight cities (Albany, Elizabeth, Erie, Paterson, Rochester, Trenton, Utica, Yonkers) record no death for two years or more (table 10). Six cities (Camden, Erie, Newark, Rochester, Utica, Yonkers) report no typhoid or diphtheria death in 1940 (table 12). It is stated that in Utica there has occurred no diphtheria death during the past seven years, during which time no typhoid death has occurred among residents and but two typhoid deaths among nonresidents. Rochester and Erie report no diphtheria death for six years; Elizabeth none in four years and but one among residents in eight years. Syracuse records but one diphtheria death (in 1939) and no typhoid death among residents during the five years 1936-1940. There were, however, three typhoid deaths and one diphtheria death among nonresidents during this period. The birth certificate form used in Syracuse provides space for the name of the physician who is to assume medical supervision of the infant. With such information the health department initiates a series of communications to parents and family physicians, timed to stimulate interest in providing protective treatments when the child is about 9 months old. Albany records no death among residents in six years (one among nonresidents in 1937). Buffalo reports one death in 1940; a continuous program of prevention with the aid of private physicians, pediatricians and child health stations. In Jersey City there were eight deaths, seven among

TABLE 2.—*Death Rates of Eighteen Cities in Middle Atlantic States from Diphtheria (Including Croup) per Hundred Thousand of Population*

	1940	1939	1935-1939	1930-1934	1925-1929	1920-1924	1915-1919	1910-1914	1905-1909	1900-1904	1895-1899	1890-1894
Rochester	0.0	0.0	0.0	0.7	7.5	16.9	12.7	22.1	32.4	32.3	45.9	96.6
Utica	0.0	0.0	0.0	1.2	13.4#	....	....	....	....	....	....	....
Erie	0.0	0.0	0.0	4.0	5.8	16.8	15.1	17.7	27.1	42.3	23.1	....
Albany	0.0	0.0	0.2*	3.0	7.5	12.8	10.4	20.0	31.6	26.9	....	....
Elizabeth	0.0	0.0	0.5†	4.5	13.2	19.2	19.3	14.8	51.7	42.4	60.5	79.3
Yonkers	0.0	0.0	0.3	0.6	10.4	17.0	17.7	25.3	....	....	....	....
Trenton	0.0	0.0	0.8	2.7	4.4	7.3	8.8	12.8	15.8	23.6	92.7‖	89.7‖
Paterson	0.0	0.0	0.9	6.3	9.1	18.5	13.5	16.1	25.5	52.9	111.8	145.4
Philadelphia	0.0	0.1	0.5	1.3	11.8	16.7	22.7	24.6	34.1	50.0	100.6	119.4
Newark	0.0	0.2	0.2	3.0	14.5	9.7	14.6	23.3	30.1	46.7	79.1	110.4
Syracuse	0.0	0.5	0.2†	0.4†	2.0	22.9	12.9	16.6	17.4	17.7	31.1	55.4
Camden	0.0	2.5†	2.7	8.1†	21.9	20.3	23.2	38.8	48.9	52.6	93.8	194.0
New York	0.1	0.3	0.6	2.2	10.7	14.0	21.8	28.0	40.0	58.0	85.8	134.4
Buffalo	0.2	0.3	0.8†	4.9	9.1	24.0	27.3	22.0	18.4	24.8	53.5	60.9
Scranton	0.7¶	0.0¶	0.7	1.7	11.7	12.3	22.1	23.4	....	....	77.8‖	48.6‖
Pittsburgh	0.7	0.4	1.3	5.1	11.5	20.1	22.3	29.3	20.4	36.9	32.9	86.4
Reading	0.9	7.2	2.5	3.6	7.3	21.1	16.9	35.7	29.2	70.1	72.0	94.1
Jersey City	2.6	2.0	2.4	6.0	11.5	18.4	21.0	23.2	32.6	57.9	85.4	108.6

* All diphtheria deaths were stated to be in nonresidents.
† One third or more of the reported diphtheria deaths were stated to be in nonresidents.
‖ Diphtheria deaths from Chapin's Municipal Sanitation.
Incomplete data.
¶ Diphtheria data furnished by Pennsylvania Department of Health, Harrisburg.

TABLE 3.—*Death Rates of Ten Cities in South Atlantic States from Diphtheria (Including Croup) per Hundred Thousand of Population*

	1940	1939	1935-1939	1930-1934	1925-1929	1920-1924	1915-1919	1910-1914	1905-1909	1900-1904	1895-1899	1890-1894
Miami	0.0	0.6*	2.2†	3.5	5.4#	....	....	....	....	....	....	....
Wilmington	0.0	1.8	1.6	6.2	10.9	11.6	15.2	18.0	27.8	50.9	84.9	83.8
Baltimore	0.3†	1.0†	1.0†	1.7	7.6	11.4	13.5	14.2	16.1	33.0	68.1	70.0
Washington	0.5	0.8†	2.8	3.7	7.1	10.5	11.9	6.9	11.2	23.5	50.9	77.9
Atlanta	0.7†	3.3†	4.6†	5.9†	7.0	13.3	10.1	12.5	14.2	11.1	10.5	8.8
Richmond	1.0†	2.6†	1.7†	3.5†	6.9	9.8	5.8	7.0	9.8	24.4	17.6	59.7
Norfolk	1.4	3.1*	2.4	4.6	4.1	4.3	4.1	6.7	17.0	....	....	....
Jacksonville	1.7†	1.3†	2.4	5.5	6.0#	...	...	...	....	....	....	....
Tampa	1.8	2.8†	3.1†	4.0	4.6	5.2	9.5#	...	....	....	....	....
Charlotte	2.0†	7.0†	6.0†	4.1	...	...	...	...	....	....	....	....

* All diphtheria deaths were stated to be in nonresidents.
† One third or more of the reported diphtheria deaths were stated to be in nonresidents.
# Incomplete data.

TABLE 4.—*Death Rates of Nineteen Cities in East North Central States from Diphtheria (Including Croup) per Hundred Thousand of Population*

	1940	1939	1935-1939	1930-1934	1925-1929	1920-1924	1915-1919	1910-1914	1905-1909	1900-1904	1895-1899	1890-1894
Grand Rapids	0.0	0.0	0.2	0.7	2.0	19.6	13.5	20.0	26.6	17.2	32.4	99.2
Canton	0.0	0.0	0.7	1.7	2.9	17.5	15.1#	....	....	....	....	....
Youngstown	0.0	0.0	0.7	3.3	10.5	18.5	11.9	40.5	33.5	28.0	17.6	28.4#
South Bend	0.0	0.0	1.0	1.3	....	....	....	....	....	....	....	....
Toledo	0.0	0.0	1.1	2.7	7.2	22.4	14.1	25.4	20.4	56.8	34.6	89.3
Akron	0.0	0.0	1.8	2.7	4.9	10.4	18.9	27.8	21.8#	....	....	....
Fort Wayne	0.0	0.0	1.9	4.0	5.1	13.1	6.3	....	....	....	....	....
Peoria	0.0	0.0	3.8	5.3	4.9	7.4	10.8	10.6	10.3#	14.0	14.6	68.0
Flint	0.0	2.0	2.8	2.7	4.5	29.9	25.5	12.7	11.0	16.8	6.9	69.2
Cleveland	0.1*	0.1	1.0	2.5	15.3	14.7	20.0	24.6	20.8	42.6	45.3	95.7
Detroit	0.2	0.4	1.1	5.2	19.7	24.3	32.2	33.3	22.6	38.5	62.9	132.9
Milwaukee	0.3	0.0	0.4	2.1	8.5	11.4	19.3	27.8	26.4	22.7	51.7	116.2
Gary	0.9	0.0	2.8	1.4	...	....	....	....	....	....	....	....
Cincinnati	0.9	2.0†	2.4†	3.1	5.2	10.6	13.2	13.9	17.0	17.3	37.3	103.7
Evansville	1.0	1.0	1.8	3.5	3.7	13.9	14.9	16.1	21.2	13.8	18.1	69.7
Chicago	1.1	1.6	2.2	4.5	11.7	17.5	31.2	37.9	27.0	33.9	69.7	117.3
Dayton	1.4†	3.3	4.3	3.6	4.6	9.4	9.3	22.1	13.3	17.2	27.4	82.9
Columbus	1.6	0.6	1.9	3.2	4.6	8.5	7.6	12.1	10.5	11.6	28.5	56.9
Indianapolis	2.6†	1.8	3.6	2.9	6.6	11.7	21.4	13.5	13.3	15.9	36.4‖	97.3#

* All diphtheria deaths were stated to be in nonresidents.
† One third or more of the reported diphtheria deaths were stated to be in nonresidents.
‖ Diphtheria deaths from Chapin's Municipal Sanitation.
Incomplete data.

TABLE 5.—*Death Rates of Six Cities in East South Central States from Diphtheria (Including Croup) per Hundred Thousand of Population*

	1940	1939	1935-1939	1930-1934	1925-1929	1920-1924	1915-1919	1910-1914	1905-1909	1900-1904	1895-1899	1890-1894
Louisville	0.6	1.6	2.2	6.2	4.6	10.4	9.5	9.0	....	....	39.0‖	48.6‖
Birmingham	0.7†	1.3*	3.1†	4.4	5.4	5.3	7.2	8.3	6.2	13.4	16.5	26.3
Chattanooga	0.8	6.3	4.0	6.8	5.9	8.7	8.9	....	....	....	....	....
Knoxville	0.9*	2.7†	8.2†	10.0	6.3	11.2	....	....	....	....	....	....
Memphis	1.7†	0.3*	2.2†	6.0	5.8	9.5	11.2	11.9	13.4	6.9	10.0	28.5
Nashville	1.8	3.0†	4.5†	8.0	11.8	8.0	8.9	7.3	10.3	13.9	30.1	28.4

* All diphtheria deaths were stated to be in nonresidents.
† One third or more of the reported diphtheria deaths were stated to be in nonresidents.
‖ Diphtheria deaths from Chapin's Municipal Sanitation.
Incomplete data.

residents. New York reports ten deaths (twenty-six in 1938, twenty-two in 1939), all among residents. It is stated that in six of the thirty health center districts, with populations ranging from 140,000 to 320,000, there have been no deaths from diphtheria during the past three years, and one of these districts with an estimated

TABLE 6.—*Death Rates of Nine Cities in West North Central States from Diphtheria (Including Croup) per Hundred Thousand of Population*

	1940	1939	1935-1939	1930-1934	1925-1929	1920-1924	1915-1919	1910-1914	1905-1909	1900-1904	1895-1899	1890-1894
Duluth	0.0	0.0	0.2	0.4	2.0	6.0	10.2	8.8	38.2	29.1	7.6	49.5
St. Paul	0.0	0.0	0.2	1.0	5.2	17.5	20.7	31.4	31.1	27.9	43.3	75.4
Des Moines	0.0	0.0	1.5	4.3	5.2	15.1	16.6	15.1	23.8#	....	....	....
Kansas City, Mo.	0.0	0.2	0.9	3.3	4.7	14.4	22.8	15.7#	....	....	....	....
Minneapolis	0.6	0.2	0.6	1.7	11.9	13.4	19.9	28.3	24.4	44.6	34.0	55.0
Wichita	0.9	0.0	1.2	5.7	4.2	....	....	....	....	....	....	....
St. Louis	1.0	1.7†	2.4†	4.8	10.3	16.1	24.4	23.7	19.4	43.3	62.9	67.7
Kansas City, Kan.	1.6	0.0	1.6	3.5	4.6	9.8	23.1	12.4#	....	....	....	....
Omaha	1.8	0.9	1.4	5.1	6.4	22.9	35.8	15.8	24.5	20.5	28.2	82.9

† One third or more of the reported diphtheria deaths were stated to be in nonresidents.
# Incomplete data.

TABLE 7.—*Death Rates of Eight Cities in West South Central States from Diphtheria (Including Croup) per Hundred Thousand of Population*

	1940	1939	1935-1939	1930-1934	1925-1929	1920-1924	1915-1919	1910-1914	1905-1909	1900-1904	1895-1899	1890-1894
Oklahoma City	0.5	0.5	2.0	5.7	10.9	....	....	....	....	....	....	....
Fort Worth	0.6*	0.6*	3.9	7.2	10.8	1.7#	2.6#	2.6	2.8	5.4	....	....
Houston	1.0	0.8	2.6	5.6	8.2	6.4	6.1	7.8	10.5	4.2#	2.4	1.8
El Paso	1.0	3.1†	4.7	8.3	7.3	20.0	17.6	29.2	....	....	....	....
Dallas	2.4†	3.1†	4.6	10.0	9.8	8.3	7.4	6.9	8.1	16.9	16.0	21.8
New Orleans	2.4†	3.9†	4.3†	5.5	8.5	6.5	11.6	19.6	10.2	11.5	17.1	51.3
San Antonio	3.6	1.2	4.1	5.7	10.3	7.7	8.7	6.7	7.6	17.1	20.6	4.4
Tulsa	4.2	0.7	1.7	6.8	12.5	8.3#	....	....	....	....	....	....

* All diphtheria deaths were stated to be in nonresidents.
† One third or more of the reported diphtheria deaths were stated to be in nonresidents.
# Incomplete data.

140,000 population has recorded no death during the past five years. Philadelphia, with no death in 1940, has joined the honor roll (table 11). Pittsburgh reports five deaths (three in 1939), four among residents.

For the nine cities of the South Atlantic states (table 3) which have been included in previous reviews, the local health officers report seventeen deaths from diphtheria in 1940, compared with forty-one in 1939. The rate for the group as a whole has declined from 1.52 in 1939 to 0.62 in 1940. The rate is now lower than that of the East North Central group (0.72) and the West North Central (0.66). Charlotte has been included in the group for the first time; however, for purposes of adequate comparison, the figures for this city have been omitted in calculating rates for the group as a whole. Two cities (Miami, Wilmington) report no death in 1940, and five other cities (Atlanta, Baltimore, Charlotte, Jacksonville, Richmond) record one third or more of deaths among nonresidents. While in 1939 four of the original cities (five with Charlotte) had rates in excess of 2.0, there was no such city in 1940. Atlanta records two deaths, one among nonresidents; Baltimore three, two among nonresidents. In January 1941 the health officer of Baltimore stated that for the second time (previous interval, September 1934 to October 1935) an unbroken year had passed without the occurrence of a death from diphtheria in a resident; however, the interval has not coincided in either instance with a calendar year. Jacksonville reports three deaths in 1940, two among residents; Richmond records two, one among residents. It is stated that in Tampa there were two deaths, in Washington three deaths, all among residents.

To the eighteen cities previously included in the East North Central group (table 4) has been added Gary, but again the figures for this city have been omitted in the tables for group comparison. The number of deaths has decreased from ninety-three to sixty-eight, the rate from 0.99 to 0.72 (table 16). In 1937 there was no city among the eighteen on the honor roll. In 1938 there were six (all remaining in 1939); in 1939 there were nine (all but one remaining in 1940); in 1940 there were nine (Akron, Canton, Flint, Fort Wayne, Grand Rapids, Peoria, South Bend, Toledo, Youngstown). Eight cities (Akron, Canton, Fort Wayne, Grand Rapids, Peoria, South Bend, Toledo, Youngstown) record no death for two years or more (table 10). Six cities (Canton, Fort Wayne, Grand Rapids, Peoria, South Bend, Youngstown) report no typhoid or diphtheria death in 1940 (table

TABLE 8.—*Death Rates of Twelve Cities in Mountain and Pacific States from Diphtheria (Including Croup) per Hundred Thousand of Population*

	1940	1939	1935-1939	1930-1934	1925-1929	1920-1924	1915-1919	1910-1914	1905-1909	1900-1904	1895-1899	1890-1894
Long Beach	0.0	0.0	0.4	0.8	2.6	10.4#	....	....	....	....	....	....
Salt Lake City	0.0	0.7	1.0	1.3	10.1	12.5	14.5	15.1	34.2	46.0	14.8	56.7#
Tacoma	0.0	0.9*	0.4*	3.9	9.3	12.4	7.7#	....	....	....	....	....
Denver	0.3	3.1	3.3	3.9	8.9	23.2	6.7	10.2	20.8	29.6	27.3	130.2
Seattle	0.5	0.3	0.4	0.4	1.4	6.6	5.5	5.2	12.5	13.4#	27.2‖	....
Spokane	0.8	0.8	0.5	0.7	7.5	11.3	4.2	7.6	25.8	....	59.5‖	18.1
San Francisco	0.9	1.1	1.0	1.2	4.6	23.0	17.0	9.2	14.4	44.2	21.6	54.8
San Diego	1.0†	1.0†	2.3	2.9	6.6	12.2	10.5	8.0	5.8	2.4	....	....
Los Angeles	1.1†	1.7	2.5	5.2	7.0	14.4	7.1	7.5	15.3	25.4	35.8	46.0
Portland	1.3	0.0	0.3	1.3	6.4	11.3	6.0	12.3	12.2	20.2	....	....
Oakland	2.0	0.6	2.5	2.0	7.4	18.8	8.1	10.3	16.1	29.1	....	....
Sacramento	5.7	1.9	3.1	4.1	...	....	....	....	....	....	....	....

* All diphtheria deaths were stated to be in nonresidents.
† One third or more of the reported diphtheria deaths were stated to be in nonresidents.
‖ Diphtheria deaths from Chapin's Municipal Sanitation.
Incomplete data.

TABLE 9.—*Two Cities with Highest Diphtheria Rate for 1940*

Sacramento	5.7
Tulsa	4.2

TABLE 10.—*Twenty-Seven Cities with No Diphtheria Deaths in 1939 and 1940*

Akron ‖	Long Beach ‡	South Bend ‖
Albany ‖	Lowell ‖	Springfield †
Canton	Lynn †	St. Paul
Des Moines †	New Bedford ‖	Toledo
Duluth ‡	New Haven ‖	Trenton
Elizabeth †	Paterson	Utica *
Erie *	Peoria ‖	Waterbury
Fort Wayne ‖	Rochester *	Yonkers ‖
Grand Rapids ‖	Somerville	Youngstown ‖

* No diphtheria deaths in seven years.
‡ No diphtheria deaths in five years.
† No diphtheria deaths in four years.
‖ No diphtheria deaths in three years.

12). Milwaukee, with no diphtheria death in 1939, records two in 1940, one among residents. Fort Wayne reports no typhoid death for six years, none from diphtheria for three; South Bend none from typhoid for five years, none from diphtheria for three. During the five years 1936-1940 there has occurred one death from diphtheria in Grand Rapids and three deaths in Canton. Chicago reports thirty-nine deaths among resi-

dents in 1940 (fifty-six in 1939). It is stated that the Chicago figures do not include deaths among Illinois residents outside of Chicago, such deaths having been allocated to the place of residence. Cincinnati reports four deaths, three among residents; Detroit three, all among residents. Cleveland records no death among residents, one in nonresidents. Gary reports one death in 1940 (none in 1939). Of ten deaths in Indianapolis, it is stated that five were among nonresidents.

TABLE 11.—*Forty Cities with No Diphtheria Deaths in 1940*

Akron	Long Beach	South Bend
Albany	Lowell	Springfield
Bridgeport	Lynn	St. Paul
Cambridge	Miami	Syracuse
Camden	New Bedford	Tacoma
Canton	New Haven	Toledo
Des Moines	Newark	Trenton
Duluth	Paterson	Utica
Elizabeth	Peoria	Waterbury
Erie	Philadelphia	Wilmington
Flint	Rochester	Worcester
Fort Wayne	Salt Lake City	Yonkers
Grand Rapids	Somerville	Youngstown
Kansas City, Mo.		

TABLE 12.—*Twenty-Four Cities with No Diphtheria and Typhoid Deaths in 1940*

Cambridge	Lowell ‡	Springfield *
Camden	Lynn †	St. Paul
Canton	Newark	Utica
Des Moines	New Bedford ‡	Waterbury *
Duluth *	New Haven	Wilmington
Erie	Peoria	Worcester
Fort Wayne ‡	Rochester	Yonkers *
Grand Rapids	South Bend ‡	Youngstown

* No diphtheria or typhoid deaths in two years.
‡ No diphtheria or typhoid deaths in three years.
† No diphtheria or typhoid death in four years.

TABLE 13.—*Four Cities in Which All Diphtheria Deaths in 1940 Were Stated to Be in Nonresidents*

Cleveland	Knoxville
Fort Worth	Providence

The cities in the East South Central states (table 5) report a rate of 1.09, compared with 2.14 in 1939, a decrease comparable to that in the South Atlantic group. In 1939 there were twenty-six deaths, in 1940 but fourteen. While there is no city in the area without a death, Knoxville records that the one death in that city occurred in a nonresident. Of thirty-one deaths reported during the quinquennium 1936-1940, nineteen were among nonresidents, illustrative of the heavy burden assumed by some urban centers for their rural neighbors. It is stated by the health officer of Knoxville that in 1940 more than 70 per cent of the preschool children are known to have received their diphtheria protection treatments. Two cities (Birmingham, Memphis) report that one third or more of the deaths occurred among nonresidents (one of two in the former, four of five in the latter). In 1939 three cities of this group reported rates in excess of 2.0, none in 1940. Chattanooga records one death, Louisville two, Nashville three, all among residents.

The nine cities in the West North Central states (table 6) report the same number of deaths (eighteen) in 1939 and 1940 (rate 0.66). While in 1939 there were five cities on the honor roll, in 1940 there were only four such cities (Des Moines, Duluth, Kansas City, Mo., St. Paul). Duluth reports no diphtheria death during the past five years and no typhoid death for two years. There has been but one typhoid death during the five year period. Des Moines records no diphtheria death for four years. Minneapolis reports three deaths in 1940, Omaha four, all among residents. It is stated that, of eight deaths in St. Louis, seven were among residents.

The eight cities of the West South Central states are the only group to report an increase in the number of deaths (forty-one in 1940, forty in 1939). The death rate has increased slightly, from 1.97 to 2.00. While there is no city in the area without a death, Fort Worth records that the one death in that city occurred in a nonresident. It is stated that the two deaths occurring in this city during the past two years have both been among nonresidents. Four cities (Dallas, New Orleans, San Antonio, Tulsa) record rates in excess

TABLE 14.—*Number of Cities with Various Diphtheria Death Rates*

	No. of Cities	40 and Over	20 and Over	10 and Over	5 and Over	Under 5	0.0
1890-1894	64	52	60	61	62	2	0
1895-1899	66	34	53	63	65	1	0
1900-1904	68	22	46	64	66	2	0
1905-1909	72	3	43	66	71	1	0
1910-1914	79	1	36	63	78	1	0
1915-1919	84	0	25	62	81	3	0
1920-1924	88	0	14	65	86	2	0
1925-1929	92	0	1	22	67	25	0
1930-1934	93	0	0	0	24	69	0
1935	93	0	0	2	17	76	19
1936	93	0	0	0	5	69	19
1937	93	0	0	0	3	70	20
1938	93	0	0	0	3	66	24
1939	93	0	0	0	2	59	32
*1940	93	0	0	0	0	53	40

* Charlotte, Gary and Sacramento omitted.

TABLE 15.—*Total Diphtheria Death Rates for Eighty-Eight Cities, 1923-1940* *

	Population	Diphtheria Deaths	Diphtheria Death Rate per 100,000 of Population
1923	31,060,848	4,078†	13.13
1924	31,722,841	3,439	10.84
1925	32,384,834	3,133	9.67
1926	33,046,827	3,106	9.40
1927	33,708,820	3,493	10.36
1928	34,370,813	3,176	9.24
1929	35,032,806	2,738	7.82
1930	35,719,180	1,827	5.22
1931	35,821,890	1,366	3.81
1932	35,916,317	1,191	3.32
1933	36,032,205	861	2.38
1934	36,166,434	821	2.27
1935	36,348,921	771	2.12‡
1936	36,549,325	551	1.51‡
1937	36,751,422	571	1.55#
1938	36,956,409	467	1.26¶
1939	37,160,779	326	0.88°
1940	37,309,215	225	0.60‖

* The five following cities are omitted from this summary because data for the full period are not available: Jacksonville, Miami, Oklahoma City, South Bend and Utica.
† Data for Fort Worth lacking.
‡ The rate for the ninety-three cities in 1935 is 2.13 (population 37,025,179, diphtheria deaths 789). The corresponding rate for 1936 is 1.52 (population 37,241,414, diphtheria deaths 567).
# Rate for ninety-three cities in 1937 was 1.55 (population 37,459,339, diphtheria deaths 583).
¶ Rate for ninety-three cities in 1938 was 1.26 (population 37,680,155, diphtheria deaths 477).
° Rate for ninety-three cities in 1939 was 0.87 (population 37,900,854, diphtheria deaths 330).
‖ Rate for ninety-three cities in 1940 was 0.60 (population 38,060,662, diphtheria deaths 229).

of 2.0. Dallas reports seven, four among residents; New Orleans twelve, only four among residents; San Antonio nine, seven among residents; Tulsa six, all among residents.

To the eleven cities previously included in the Mountain and Pacific group (table 8) has been added Sacramento, but the figures for this city have been omitted in the tables for group comparison. For the eleven cities the health officers report thirty-nine deaths in 1940 (fifty in 1939). The rate for 1940 (0.93) is lower than that of 1939 (1.20). The group as a whole stands in sixth place. There are three cities (Long Beach, Salt Lake City, Tacoma) with no death in 1940. Long Beach records no death for five years; Tacoma two deaths, both among nonresidents, for the same period. Two cities (Oakland, Sacramento) record a rate for 1940 in excess of 2.0. Oakland reports six deaths, all among residents; Sacramento six, five among residents. Los Angeles records seventeen deaths, nine among residents; Portland four, two among residents; San Francisco six, four among residents. The health officer of the latter city reports a shift in the age incidence of diphtheria toward adults in recent years.

TABLE 16.—*Total Diphtheria Death Rates per Hundred Thousand of Population for Ninety-Three Cities According to Geographic Divisions*

		Diphtheria Deaths		Diphtheria Death Rates				
	Population	1940	1939	1940	1939	1935-1939	1930-1934	1925-1929
New England.....	2,579,152	6	13	0.23	0.50	0.85	3.38	8.34
Middle Atlantic.....	13,129,185	26	49	0.20	0.37	0.65	2.50	9.97
South Atlantic.....	2,727,985	17	41	0.62	1.52	2.18	3.54	7.37*
East North Central..	9,386,378	68	93	0.72	0.99	1.82	3.66	11.21†
East South Central..	1,286,747	14	26	1.09	2.14	3.37	6.36	6.34
West North Central..	2,716,484	18	18	0.66	0.66	1.33	3.22	7.82
West South Central..	2,048,692	41	40	2.00	1.97	3.85	6.55	9.24‡
Mountain and Pacific	4,186,039	39	50	0.93	1.20	1.71	2.69	6.28

* Lacks data for 1925 for Jacksonville and Miami.
† Lacks data for South Bend.
‡ Lacks data for Oklahoma City for 1925 and 1926.

Of the entire ninety-three cities there are none with a rate of 5.0 and over (table 14), although one of the three newly added cities (Sacramento) reports a rate of 5.7. Only one city of the original group, Tulsa (rate 4.2), records a rate in excess of 4.0. The number of cities with no deaths from diphtheria has increased by eight; that is, from thirty-two to forty (there were twenty-four such cities in 1938). For the eighty-eight cities (table 15) for which data are available since 1923, there occurred 225 deaths from diphtheria in 1940, which is by far the lowest of record (326 in 1939; 467 in 1938). The rate for this group of cities is for the second time less than 1.0. The rate for the ninety-three cities is also below 1.0 (0.60). The actual number of diphtheria deaths has decreased by one hundred and one (from 330 to 229). This is a remarkable record.

Intensive protection programs are being carried on in all parts of the country, especially among the preschool children. The family physician continues to become a more important part of this program and is giving more protective treatments in his own office. The evidence continues to indicate that the protection programs so extensively maintained are resulting in a definite lower death rate from diphtheria. May the good work continue!

THE TRANSMISSION OF CERTAIN INFECTIONS OF RESPIRATORY ORIGIN

A CRITICAL REVIEW

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At this moment, because of the exigencies of the defense situation, a part of our population is being congregated under conditions highly conducive to the spread of respiratory infections. Furthermore, since even in normal times respiratory infections, both major and minor, are probably responsible for the greater part of all illness in every age group,[1] knowledge of the modes of spread of these infections is of unusual importance.

The older or "contact" theory of the spread of respiratory infections seemed to preclude the possibility of direct intervention in the infection cycle. As a result, efforts toward control of these infections have been directed largely along immunologic lines. In spite of the great amount of energy expended in these efforts, they have, on the whole, had little success. On the other hand, the newer or "air borne" hypothesis suggests other means of control as a reward for its demonstration and thus contributes a new approach to the problem of the prevention of respiratory infections.

The contact theory explains dissemination of respiratory infections as entirely one of person to person transfer, either by direct contact or by droplets. That this route of infection does in fact operate has been suggested by clinical observation. Flügge[2] and his school at the end of the last century showed that bacteria in droplets emitted by coughing could be recovered only at relatively short distances from their point of origin. These findings received apparent confirmation in practice, in the successful use of the so-called method of barrier nursing. By the proper spacing of beds the incidence of cross infections could be reduced; but it was soon discovered that this method did not prevent the spread of such diseases as chickenpox and measles.

The apparent confirmation of the direct contact theory did not satisfy all investigators, and a renascence of interest in the mode of spread of respiratory infections has appeared in recent years in the work of clinicians and laboratory workers in several countries, among them Trillat in France, Wells and De Lee in this country, and Cruikshank and Allison in England. A synthesis of their findings and those of others gives us a hypothesis which, while it does not invalidate the droplet idea per se, brings into question its relative significance. Stated simply, the indirect or air borne hypothesis postulates that the greatest spread of respiratory infection is produced by small dried droplets floating in air for relatively long times and distances, or by the resuspension of dried droplets in air after they have settled to surfaces such as floors, clothing and bedclothes. This hypothesis has been advanced by three lines of investigation: 1. Surveys of microorganisms from the upper respiratory tract of man in his indoor environment and laboratory studies on the fate of micro-organisms in simulated room environments

From the DeLamar Institute of Public Health of the Columbia University College of Physicians and Surgeons.

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2. Flügge, C.: Ueber Luftinfection, Ztschr. f. Hyg. u. Infectionskr. **25**: 179, 1897, Die Verbreitung der Phthise durch staubförmiges Sputum und durch beim Husten verspritzte Tröpfchen, ibid. **30**: 107, 1899.

as well as experimental transmission of virus infections to animals via the air. 2. The development of methods for the identification of individual strains of streptococci by refined serologic technics similar to those previously established for pneumococci, as well as the classification of the diphtheria bacillus into three types, and the application of these means to the study of the spread of the organisms mentioned. 3. The development of several effective control measures based on the assumption that respiratory infections are essentially air borne. Each of these may now be discussed in turn.

LABORATORY STUDIES

Trillat [3] since 1909 has studied various aspects of the problem of air borne infection. Among other phases he has investigated the effect of physical and chemical factors on the properties of microbial droplets suspended in air, the transmission of infection to animals by the air borne route and, lately, means for the prevention of air borne infection. For many years when the air borne hypothesis was in an advanced stage of desuetude his was the only laboratory actively interested in the problem. However, the investigations of Wells in this country starting in 1933 furnished the stimulus which is largely responsible for the current interest in this hypothesis. Wells [4] showed, by means of a centrifuge apparatus which he developed, that when bacteria of the types which produce disease in the upper respiratory tract are sprayed into the air they can be recovered from it for many hours afterward. He also revived a hypothesis of Gordon that some indication of the extent of nasopharyngeal contamination could be obtained by estimation of the number of alpha hemolytic streptococci of the throat found in the air of enclosed places. At Wells's suggestion an extended survey of the distribution of alpha hemolytic streptococci in the air of schools, theaters and a subway was undertaken in New York City with the aid of the air centrifuge (Buchbinder, Solowey and Solotorovsky [5]). Some two thousand five hundred samples were analyzed. It was found that alpha hemolytic streptococci of nasopharyngeal origin were widely distributed in the air of these enclosed places and that their numbers in each type of location varied directly with conditions of occupancy and ventilation. In addition, although beta hemolytic streptococci of group A were relatively rare in "normal" air, forty-six such strains obtained from the air were found to be indistinguishable in several pathogenic properties from a similar number of strains of group A streptococci which had been isolated directly from disease processes.

Since then there have been several studies on methods for the recovery of bacteria from air. Wells [6] has suggested a simplified technic for bacterial air analysis with the use of the air centrifuge; Hollaender and Dalla Valle [7] have developed a combined Petri plate and suction device which they have used in one study on the efficiency of filters and in another on the transmission of bacteria by ventilating systems; and Phelps and Buchbinder [8] have found that the Petri dish technic alone is suitable for some types of air analysis.

The suggestive findings of the New York City survey led to an extensive laboratory investigation of the fate of streptococci in simulated room environments. It was determined that streptococci artificially sneezed into air settled out geometrically on agar plates at a rate of about 20 per cent an hour, which resulted in a residual population in the air at the end of twenty-four hours of about 0.5 per cent of the initial number capable of settling (Phelps and Buchbinder [8]). After settling had occurred it was found that streptococci died at geometric rates and that they could be recovered from the floor of a dark room for extended periods. Appreciable numbers of organisms were sometimes still alive several weeks after settling from the air (Buchbinder and Phelps [9]). Furthermore it was found by an extended investigation of several pathogenic properties, such as mouse virulence, ability to grow in defibrinated human blood and the fibrinolysis of clotted human blood, that these properties were never more than slightly impaired by room sojourn (Buchbinder, Solowey, Solotorovsky; Buchbinder, Solotorovsky, Solowey and Ruhl-Koupal [10]).

Another investigation, whose findings are of significance if the air borne route is important in the dissemination of infection, is one in which the effect of sunlight and daylight on streptococci and pneumococci in a simulated room environment was studied (Buchbinder, Solowey and Phelps [11]). Although it has been known for a long time that the visible spectrum, particularly the blue region, exerts a bactericidal effect (Downes and Blunt and others [12]) research on the

3. Trillat has had numerous papers published in the Comptes rendus de l'Académie des sciences and in other French journals. His first paper was perhaps in 1909 (Trillat, A., and Santon: Action des gaz putrides sur les microbes, Compt. rend. Acad. d. sc. **149:** 875, 1909). His latest paper is Sur le mécanisme de transmission des maladies transmissibles par l'air et sur les aérosols microbiens, Arch. Inst. Pasteur Tunis **29:** 294, 1940.

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lethal effects of sunlight has largely been directed toward the much more potent ultraviolet region of the invisible spectrum. This apparent lack of appreciation of the disinfecting power of visible light may be due in part to the fact, as stated by Duggar,[13] that in the early days "extravagant claims were made regarding the disinfecting value of even diffuse light of low intensity, and such extreme views were not overcome for a period of years," and in part to the absence of a quantitative technic for the estimation of the admittedly weaker activity of daylight. Indeed, some of the studies on the quantitative germicidal effect of ultraviolet light are subject to criticism in that the organisms were tested under conditions which did not simulate their natural environment. In the present studies the effects of sunlight and daylight which had passed through the glass of a window and the glass covers of Petri plates were tested on streptococci and pneumococci which had settled out of the air into the bottoms of Petri plates. It was found that under these conditions diffuse daylight was a potent lethal agent. Thus 50 per cent of the organisms of a short chained strain of alpha hemolytic streptococcus died in about three quarters of an hour, as did strains of pneumococci of types I, II and III. Likewise it was observed that the 50 per cent lethality zone of strains of group A beta hemolytic streptococci was reached after somewhat longer intervals, which appeared to have been due, in part at least, to the greater chain length of these strains. The lethal effect of daylight was found to be dependent on both quantitative and qualitative factors. Diffuse daylight from blue skies exerted a maximal effect per foot candle, whereas light from gray skies produced a minimal one. The total lethality even under overcast skies, however, was not insignificant. This was so because of increased reflection from the clouds; i. e., the total number of foot-candles available was greater. Direct sunlight through glass under similar conditions was about ten times as potent as diffuse daylight, 50 per cent of the chains of the alpha hemolytic streptococcus strain being killed in about five minutes. Lastly, the now relatively common tubular fluorescent lamp was found to exert a lethal effect per foot candle which was only slightly less than that of daylight. It may be concluded, then, that if the air borne route for respiratory infections is important (1) the concentration in our environment of organisms of the types which cause these infections is reduced by natural daylight and sunlight, and (2) this suggests the planning of a maximum of window space in new hospitals, schools and homes.

Still another field of laboratory investigation which has been barely invaded is that of the mode of spread of virus infections of the respiratory tract. Some suggestive clinical evidence for the air borne transmission of psittacosis to man (McCoy, Stimson[14]) and canine distemper to dogs and ferrets (Dunkin and Laidlaw[15]) has been adduced. In addition, as will be discussed subsequently, there is indirect evidence that chickenpox virus also travels through the air. However, just as there is little concrete knowledge of the reservoirs for virus infection so there is little more than this circumstantial evidence for the routes by which virus infections spread. This subject is undeveloped because means for the laboratory study of viruses, unlike those for bacteria, are largely inadequate. Nevertheless some progress has been made. Wells and Brown,[16] by collecting influenza virus with the air centrifuge after spraying, and transferring it to ferrets, were able to recover the virus for thirty but not for sixty minutes. Similarly, Trillat and Beauvillain[17] reported the infection of ferrets exposed to a spray of influenza virus. The first study by a quantitative technic of the settling of virus particles from air has recently been made (Buchbinder and Solotorovsky[18]). This was done by exposing the intact chorioallantoic membrane of the developing chick embryo to vaccinia virus sprayed into air, resealing the egg and counting the pocks which developed after three additional days' incubation. It was found that vaccinia virus could be recovered for at least eight hours after being sprayed into the air and that the virus seemed to settle out at a faster rate than did bacteria, a finding which may indicate a more rapid death rate for the virus. This method or some adaptation of it may furnish a useful tool for further study of the general problem of the mode of transmission of virus infections.

In summary, these studies furnish ample experimental basis for the air borne hypothesis. They demonstrate that such common pathogens as the streptococcus and pneumococcus may persist in air and maintain their virulence for relatively long time periods after being sneezed artificially, and that a similar phenomenon, perhaps of shorter duration, may also occur with certain viruses.

CLINICAL STUDIES

Although relatively little study has been made of the manner of spread of streptococcic, pneumococcic and diphtheritic infections in the population at large, infections developing in hospitals may be taken as illustrative of the general problem. Such infections constitute in their own right a serious problem in hospital management. The institutions in which new infections are of the greatest importance are isolation, children's and maternity hospitals. In the surgical and medical wards of general hospitals, as might be expected, the problem is somewhat less important.

New means for the identification of streptococci were furnished by the pioneering efforts of Lancefield[19] in distinguishing those strains infecting man from others and by the systematization of the serologic types causing human disease by Griffith.[20] When streptococci of several serologic types are recovered from the air of a room it is now sometimes possible to identify the person or persons from whom each was derived. Likewise studies of the spread of infection, under the special conditions existing in a hospital ward, may provide data on the relative likelihood of direct person to person transfer or of the alternative indirect mechanism.

13. Duggar, B. M.: Effects of Radiation on Bacteria, in Biological Effects of Radiation, New York, McGraw-Hill Book Company, Inc., 1936, vol. 2, chapter 36, p. 1120.

14. McCoy, G. W.: Psittacosis Among the Personnel of the Hygienic Laboratory, J. Infect. Dis. **55**: 156 (Sept.-Oct.) 1934. Stimson, A. M.: Bacteriological Investigations of the United States Public Health Service, Pub. Health Rep., 1938, supp. 141, p. 48.

15. Dunkin, G. W., and Laidlaw, P. P.: Studies in Dog Distemper: I. Dog Distemper in the Ferret, J. Comp. Path. & Therap. **39**: 201, 1926; II. Experimental Distemper in the Dog, ibid. **39**: 213, 1926.

16. Wells, W. F., and Brown, H. W.: Recovery of Influenza Virus Suspended in Air and Its Destruction by Ultraviolet Radiation, Am. J. Hyg. **24**: 407 (Sept.) 1936.

17. Trillat, A., and Beauvillain: Essai de transmission aérienne de la grippe au furet par voie pulmonaire ou oculaire, Compt. rend. Acad. d. sc. **205**: 1186 (Dec. 6) 1937.

18. Buchbinder, Leon, and Solotorovsky, Morris: Studies on Micro-Organisms in Simulated Room Environments: VI. The Disappearance of Vaccinia Virus from Air, J. Bact. **42**: 635 (Nov.) 1941.

19. Lancefield, R. C.: A Serological Differentiation of Human and Other Groups of Hemolytic Streptococci, J. Exper. Med. **57**: 571 (April) 1933.

20. Griffith, F.: The Serological Classification of Streptococcus Pyogenes, J. Hyg. **34**: 542 (Dec.) 1934.

STREPTOCOCCIC INFECTIONS

Scarlet Fever Wards.—The most significant studies have been carried out in scarlet fever wards of isolation hospitals. In these wards the occurrence of so-called complications is a major problem. As indicated by de Waal,[21] 28 per cent of more than 2,000 cases studied over a fifteen month period in the Edinburgh Fever Hospital presented complications which necessitated an estimated fourteen thousand four hundred extra days in the hospital for the patients involved.

TABLE 1.—*The Relation of the Number of Swabs Taken to the Percentage Incidence of New Serologic Types of Streptococci in the Upper Respiratory Tract of Patients in Scarlet Fever Wards*

Authors	No. of Patients	Per Cent with New Type
Gunn and Griffith	100 [1]	50
Allison and Gunn	200 [1]	46
Allison and Brown	100 [2]	57
	47 [3]	70
Green	1,062 [2]	10
White and others	2,203 [4]	55
De Waal	254 [5]	76
	86 [6]	75

Presence of new type determined by throat swab:
1. Weekly during hospitalization.
2. On discharge from hospital.
3. Twice weekly during hospitalization.
4. After 3½ weeks of hospitalization.
5. After more than 2 weeks of hospitalization.
6. Daily during entire period of hospitalization.

It has been found, as was first suggested by Smith,[22] that the majority of these complications are actually new infections by a strain of streptococcus serologically distinct from the patient's original one, whose source can usually be traced to some other individual in the hospital, in most instances a fellow patient. Thus a new strain was found to be responsible for the complications in 18 of 20 instances intensively studied by Brown and Allison [23] and in 61.5 per cent (280 of 450) instances reported by de Waal.[21] Furthermore, it has become evident that the incidence of clinical complications does not furnish complete evidence of the actual spread of streptococci through a ward. A bacteriologic study of all cases, complicated or not, reveals a still higher incidence of new infection, which includes cases in which new serologic types are harbored in the absence of clinical symptoms [24] (table 1).

In the opinion of several investigators, direct contact between patients via droplets or by more intimate association is the most important route of spread of ward infections. Thus Gunn and Griffith [24] found that 13 of 50 patients studied acquired their infection while in bed, whereas 37 did not show a new type until they were ambulant, from which they concluded that the organisms were spread by the direct mingling of patients. Likewise Allison and Brown,[24] from similar observations, came to the same conclusion: "The most frequent mode of transmission of reinfection appears to be by direct contact of patient with patient." De Waal,[21] whose experience was comparable, was also of a similar although more qualified opinion: "Direct contact seems to play some part in the transmission of streptococci. . . ."

On the other hand, the data of these authors and others contains evidence in favor of the air borne hypothesis. In the first place streptococci can be recovered from the air of scarlet fever wards in relatively large numbers (Vas; Friedemann and Deicher [25]). Brown and Allison [23] exposed Petri plates to the air of scarlet fever wards at three time intervals during twenty-four hours. Their results indicated that "Hemolytic streptococci are widespread in the ward air and the serological types identified were not confined to the neighborhood of patients infected with a particular type. The degree of infection of air with hemolytic streptococci showed considerable variation during the twenty-four hours. During the night infection was absent or negligible; in the morning there was a steep rise, followed by a slight fall in the degree of infection during the early afternoon. This variation is probably associated with the degree of air movement in the ward produced by the ward staff in the execution of their duties." The number of organisms actually breathed by an individual in such a ward can be determined in a crude way. It can be computed by using a set of data on page 8 of the report of Brown and Allison that in a twenty-four hour period, assuming a settling rate of streptococci from air of 10 inches an hour, approximately thirty thousand organisms might be breathed by each child. The settling rate used is derived from the study of Phelps and Buchbinder [8] on the settling rates of streptococci artificially sneezed into the air of a quiet room. This value, it may be noted, is likely to be greater in an occupied and busy ward. Nevertheless, even if a settling rate as high as 300 inches an hour is postulated, each child might still breathe one thousand organisms a day.

TABLE 2.—*The Incidence of Throat Swabs Positive for Streptococci on Admission to and Discharge from a Hospital (Green, 1937)*

	Total No. of Cases		0	+	++	+++
Admission	1,875	Cases	294	238	689	654
		Per cent	15.7	12.7	36.7 84.3	34.8
Discharge	1,548	Cases	978	250	227	84
		Per cent	63.2	16.7	14.7 36.8	5.4

0 = no growth or no streptococci detected on plate; + = less than 10 colonies on plate; ++ = 10 to 20 colonies on plate; +++ = more than 20 colonies per plate.

The integration of several other groups of data indicates the probability that reinfection with streptococci usually can occur only after a week or more of hospitalization. It is generally agreed that during hospitalization the number of colonies of streptococci isolated on Petri plates from a swab of a patient's throat decreases

21. de Waal, H. L.: The Serological Types of Hemolytic Streptococci in Relation to the Epidemiology of Scarlet Fever and Its Complications, J. Hyg. **40:** 172 (March) 1940.

22. Smith, J.: The Serological Classification of Hemolytic Streptococci Obtained from Cases of Scarlet Fever, J. Hyg. **25:** 165 (July) 1926; Further Studies on the Serological Classification of Hemolytic Streptococci, ibid. **26:** 420, 1927.

23. Brown, W. A., and Allison, V. D.: Infection of the Air of Scarlet Fever Wards with Streptococcus Pyogenes, J. Hyg. **37:** 1 (Jan.) 1937.

24. Gunn, W., and Griffith, F.: Bacteriological and Clinical Study of One Hundred Cases of Scarlet Fever, J. Hyg. **28:** 250, 1928. Allison, V. D., and Gunn, W.: The Epidemiology of Streptococcal Infections, Proc. Roy. Soc. Med. **25:** 927, 1932. Allison, V. D., and Brown, W. A.: Reinfection as a Cause of Complications and Relapses in Scarlet Fever Wards, J. Hyg. **37:** 153 (April) 1937. Green, C. A.: The Serological Types of Hemolytic Streptococci in Epidemic Scarlatina, ibid. **37:** 318 (April) 1937. White, C.; Rudd, G. V.; Ward, H. K.; Wilson, F. H., and Symington, N. J.: The Serological Types of Hemolytic Streptococci Causing Scarlet Fever in Sydney, M. J. Australia, **1:** 96 (Jan. 21) 1939. de Waal.[21]

25. Vas, B.: Ueber das Vorkommen von Scharlachstreptokokken in der Luft., Zentralbl. f. Bakt. O. (Abt. 1) **98:** 159, 1926. Friedemann, U., and Deicher, H.: Die Uebertragung des Scharlachs, Deutsche med. Wchnschr. **52:** 2147 (Dec. 17) 1926.

progressively with time (Gunn and Griffith;[24] Keogh, MacDonald, Battle, Simons and Williams[26]). Green[24] has compared the number of positive throats, as well as the number of colonies per positive plate, of groups of more than 1,500 patients on admission to and discharge from a hospital (table 2). Green's data, however, are probably complicated by the fact that a number of the patients were unquestionably reinfected during hospitalization, so that the figures obtained on discharge were probably higher than they would have been if reinfection had not occurred. Perhaps more satisfactory data for analysis are furnished by de Waal,[21] who studied a series of 30 patients who did not suffer any complications while in the hospital. It is not entirely clear whether this means that no new strains were isolated. De Waal found that the percentage of negative throat swabs taken at the end of each five weeks gradually increased (table 3).

Secondly a series of observations suggests that the presence of one strain of streptococcus in a throat may militate against the implantation of a different strain, at least in scarlet fever wards. Allison and Brown[24] observed that during thirteen weeks a total of eleven primary infecting strains were found in a ward at one time or another, an average of about six strains being present during each of the first ten weeks. Nevertheless, of 33 reinfected patients, 21 acquired only one new type, and the remaining 12 acquired from two to four. De Waal states, moreover, that "Once a new type appeared in the throat of a patient, it tended to persist either alone or in conjunction with the original type. When a third type occurred, its appearance was either temporary or, if it persisted, the other types disappeared."

TABLE 3.—*Comparison by Weeks of the Percentage of Patients with New Types of Streptococci in Throat and Percentage with No Streptococci in Throat in Absence of Complications*

Author	Number of New Cases	Per Cent	Swabbed During 1st Wk.	2d Wk.	3d Wk.	4th Wk.
Allison and Brown	47	With new types....	2.1	25.5	61.7	70.2
De Waal...	30	Negative in absence of complications	3.3	16.3	39.9	66.7

This point is further amplified when the liberty is taken of placing in juxtaposition for purposes of comparison the findings of de Waal and data taken from Allison and Brown. In table 3 de Waal's data on uncomplicated cases, given in terms of percentage incidence by weeks of negative throats, are placed alongside those of Allison and Brown, given as percentage incidence of new serologic types found in the throats in complicated cases during similar periods. It is seen that during the first week almost all the throats are still positive for the original strain and that very few new strains are found. Likewise, during the first week and throughout succeeding weeks a positive correlation is noted between the presence of new strains in complicated cases and that of negative throat swabs in uncomplicated ones. This may be taken as suggesting that, as the incidence of throats still harboring their primary strains decreases, the proportion of throats showing new strains increases.

However, it is also noted that, from the second week onward, the percentages given by Allison and Brown are higher than those of de Waal. If these data may be regarded as comparable, the higher values for reinfection may be explained on the ground that new infections sometimes occur before the original strain disappears from the throat. Such a finding has actually been reported by de Waal:[21] "In the majority of patients before new strains become established in their throats, a period of some days elapsed during which the previous strain appeared to decrease or die out. In [some] cases, . . . however, one type was suddenly replaced by another."

All these observations may now be summarized as follows: 1. The number of organisms of the original infecting strain present in the throat of a scarlet fever patient tends to decrease with time. 2. Those throats reinfected during hospitalization in most instances show only one new type despite the fact that several are available in the environment. 3. The presence of a strain in the throat in large numbers during the first week of hospitalization seems to be antagonistic to the implantation of a new strain.

Synthesis of these findings suggests that reinfection and the resultant complications could not occur until the second or third week of hospitalization because the patient is not susceptible to reinfection until that time. The recovery of large numbers of streptococci from the air of the wards indicates that probably at most times enough organisms of the proper serologic types are present to account for all the new infections. The findings of Buchbinder and his associates, previously mentioned, on the comparative stability of several pathogenic properties of streptococci in simulated room environments provide grounds for assuming that the pathogenicity of these strains is not lost during their sojourn in man's environment.

According to the air borne theory one would thus ascribe the low incidence of reinfections during the first week of hospitalization to the fact that the presence of the original strain in relatively large numbers in almost all throats during this period would interfere with the implantation of new strains, even in the presence of large numbers of suitable pathogens in the air. The direct contact theory would attribute this initial low incidence to the absence of contact between patients while they were still in bed. Further light may be cast on this point when children not infected with streptococci are placed in a ward in which streptococci are present (Allison[27]). Nineteen children with measles were admitted to a hospital ward, and on admission 6 of them were found to be carrying streptococci in their throats. One week later 7 of the 13 children whose throats did not yield streptococci on admission were found to be streptococcus carriers, six of these strains being of the same serologic types as those of the children found to be positive on admission to the ward. All these children had remained in bed during the entire week. Thus about half of the streptococcus negative children became positive in one week in the absence of contact. This observation runs counter to the hypothesis that only ambulatory patients are subject to reinfection but is quite compatible with the air borne hypothesis, since the possibility of what might be called antagonism between strains, noticed in the first week in scarlet fever wards, is nonoperative because of the absence of an original streptococcic infection.

26. Keogh, E. V.; MacDonald, Ian; Battle, Joan; Simons, R. T., and Williams, Stanley: Some Factors Influencing the Spread of Scarlet Fever in an Institution, J. Hyg. **39**: 664 (Nov.) 1939. Green.[24]

27. Allison, V. D.: Streptococcal Infections, Lancet **1**: 1067 (May 7) 1938.

The fact that most reinfections do not occur before the second or third week despite the large number of organisms in the air at all times is explained on the air borne hypothesis, as previously mentioned, by the occurrence of renewed susceptibility to infection at that time. If the same fact is used to support the direct contact theory, a fortuitous conjunction of renewed susceptibility to infection and opportunity for contact by patients becoming ambulatory at this time must be assumed.

It is of interest that, although Brown and Allison regarded direct contact as most important in the spread of reinfections, they nevertheless concluded that because of the finding of large numbers of streptococci in the air the possibility of infection via the air could not be dismissed. Likewise de Waal considered that not all ambulatory patients acquired their new infections by contact, since "a number of convalescent patients who were going about the ward contracted complications almost simultaneously with type 6 streptococci, and the only source of infection in the ward at the time was an isolated bed patient with rhinitis, from whom type 6 had been isolated." It might be added parenthetically that Okell and Elliot,[28] in studying the spread of streptococcic infection in an otorhinologic ward, found streptococci on the inside but not outside surface of a three panel glass screen surrounding 1 patient's bed. They were also able to recover the same strain of streptococcus, however, on Petri plates placed on the floor a few feet outside the screen.

There have been no extensive studies on the possibility of transfer of infection from patient to patient by nurses. Allison and Brown found, as might be expected, that strains of streptococci prevalent in the ward could be recovered at times from the throats of some of the nurses. These authors seem to have made no attempt to assess the importance of the spread of infection through this route. It is known, however, that patients nursed in isolated cubicles show an almost negligible incidence of reinfection as compared with those treated in multiple bed wards. Lichtenstein[29] studied two groups of patients, 171 in each, who were so divided, and found that no patients relapsed who were nursed alone or in a double bed ward with another member of the patient's family, who presumably was infected with the same type. In 10 additional cases relapse did occur in the isolation pavilion, but in each instance the relapse occurred in a double bed room, whose occupants were presumably unrelated. In the multiple bed, or control, series there were 21 relapses. Similarly Allison and Brown swabbed 16 patients, nursed in isolated cubicles, twice weekly from admission to discharge. With 1 exception only the primary infecting type of streptococcus was recovered from each of these patients. The exception was a patient who had had two strains on admission, one of which disappeared and later reappeared when the strain presumably responsible for the scarlet fever disappeared. These findings can be taken to indicate that nurse contact, which occurs in both groups, is not an important factor in the transmission of infection.

Streptococcic Infections in Other Hospitals.—The following studies of new infections in other hospitals are not as complete as those which have been discussed. It is also possible that streptococci may not be as ubiquitous in these places since, unlike the condition in scarlet fever wards, not every patient is primarily infected with streptococci.

Maternity Hospitals: The most important single cause of severe illness in postparturient women is streptococcic infection, and the greatest source of this infection after hospital delivery is the hospital personnel or patients, either directly or indirectly.

Dora C. Colebrook[30] has tabulated the findings of several investigators on the streptococcic morbidity and mortality of women entering a hospital because of some complication after delivery. A summary of her tables shows that 49.4 per cent (546 of 1,106) were infected by the streptococcus, that 26.4 per cent (128 of 485) died and that the streptococcus was responsible for 79.5 per cent (128 of 161) of all deaths among the women. She has also estimated that if streptococcic infections after childbirth were prevented there would be 576 less deaths and 2,304 less cases of severe nonfatal illness among mothers annually in England and Wales. In addition Leonard Colebrook[31] has made the more immediate suggestion that, if what was accomplished by preventive measures in a single London hospital was extended to other institutions, deaths and illness of postparturient women due to streptococcic infection would be reduced by at least one half.

Autoinfection is not the major source of puerperal infection. The first experimental evidence indicating that the major source of infection is external was presented by Kanter and Pilot[32] in 1924, and since then the fact has been amply established.[33] Dora C. Colebrook[30] has summarized the experience of others, involving several thousand cases, which showed that (1) at various stages before delivery the incidence of streptococci in the genital tract was only between 2 and 3 per cent, and (2) that but few of these streptococcus positive women had any severe febrile experience during the puerperium. The latter finding may be explained by the fact, as shown by Lancefield and Hare, that most of the streptococci in the normal vagina are of the relatively nonpathogenic group B. On the other hand, Rolfs and others[34] found group A streptococci in the throats of about 7 per cent of five hundred women on admission to a maternity hospital, which is within the range of that found in the population at large.

Relatively thorough bacteriologic and epidemiologic studies have been made by Smith[33] and by Dora C. Colebrook.[30] The possible source of infection was found in about 80 per cent of the persons studied to be in the nose and throat of patients or contacts. The same serologic type as that causing the infection was found

28. Okell, C. C., and Elliot, S. D.: Cross Infection with Hemolytic Streptococci in Otorhinological Wards, Lancet **2**: 836 (Oct. 10) 1936.

29. Lichtenstein, A.: Studies in Scarlet Fever: VIII. Further Investigations into Relapses, Their Nature and Prevention, Acta paediat. **12**: 75, 1931; IX. A Note on the Effect of Individual Isolation on the Course and Complications of Scarlet Fever, ibid. **12**: 95, 1931.

30. Colebrook, Dora C.: The Source of Infection in Puerperal Fever Due to Hemolytic Streptococci, Medical Research Council, Special Report Series, no. 205, London, His Majesty's Stationery Office, 1935.

31. Colebrook, Leonard: The Prevention of Puerperal Sepsis, J. Obst. & Gynaec. Brit. Emp. **43**: 691 (Aug.) 1936.

32. Kanter, A. E., and Pilot, Isadore: Hemolytic Streptococci and Their Relation to Pregnancy and the Puerperium, Surg., Gynec. & Obst. **38**: 96 (Jan.) 1924.

33. King, W. W.: Throat Infections as an Etiological Factor in Puerperal Fever, with a Report of Twenty-Four Cases, Brit. M. J. **1**: 533 (March 22) 1930. Williams, J. T.: The Relation of Respiratory Infections to Puerperal Infection, J. A. M. A. **99**: 1991 (Dec. 10) 1932. Taylor, J., and Wright, H. D.: The Nature and Sources of Infection in Puerperal Fever, J. Obst. & Gynaec. Brit. Emp. **37**: 213, 1930. Smith, John: A Further Investigation into the Source of Infection in Puerperal Fever, J. Obst. & Gynaec. Brit. Emp. **40**: 991 (Oct.) 1933. Report No. 1, Scottish Scientific Advisory Committee, Department of Health for Scotland, 1931. Paine, C. G.: The Etiology of Puerperal Infection with Special Reference to Droplet Infection, Brit. M. J. **1**: 243 (Feb. 9) 1935.

34. Rolfs, F. O.; Trussell, R. E., and Plass, E. D.: Serological Study of Hemolytic Streptococci from the Throat, Nose and Vagina of Antepartum Obstetric Patients, Am. J. Obst. & Gynec. **35**: 1009 (June) 1938. Lancefield, R. C., and Hare, R.: The Serological Differentiation of Pathogenic and Nonpathogenic Strains of Hemolytic Streptococci from Parturient Women, J. Exper. Med. **61**: 335 (March) 1935.

in contacts in 62 per cent of the cases. In Colebrook's series, which was intensively studied, infection was assigned in 39 cases to several sources as follows: attendants 24, infection existing at home 9 and the patient herself 6. Congdon's [35] results were exceptional in that by agglutinin absorption the strains causing twelve infections were found to be present in 8 instances in the patients' throat and in only 6 instances in those of attendants. Nevertheless, even he found a larger than normal percentage of carriers of hemolytic streptococci among attendants (27 per cent). Hare and Colebrook [36] had previously reported 30 to 40 per cent, and Bryce and Tewsley [37] have since obtained a value of 22 per cent. As mentioned previously, Rolfs and others found a normal incidence of 7 per cent in patients on admission.

No final conclusion can be drawn at present as to the relative importance of contact and air borne infection in maternity cases. Perhaps comprehensive studies, such as the study of Brown and Allison in a scarlet fever hospital, would provide the necessary data. Indications of the possible significance of air borne infections are furnished, however, by the findings of White [38] and of Cruickshank and Godber.[39] White observed that streptococci could be isolated from the dust of twenty-seven single bed rooms; in most instances the organisms recovered were of the same serologic type as that causing the puerperal infection of the patient concerned. She also found that, by sweeping the floor, streptococci could be recovered from the air of these rooms for several days after they had been vacated. A person who swept one of the floors came down with an acute pharyngitis and adenitis, caused by the same serologic type as that isolated from the patient who had previously occupied the room. This occurred despite the fact that the sweeper had been masked. Cruickshank and Godber investigated a small outbreak of puerperal fever in the maternity ward of a general hospital. In this instance the infection was introduced to the hospital by a patient who, infected on admission, was delivered and remained in the main maternity ward for two days before being removed to isolation. On the day she was removed and on the following day two other women who had been delivered in different labor rooms, and with different nurses, were placed in the same ward. These women became febrile one and two days later and were found to be infected with the same serologic type as the first patient. They were both sent to isolation on the day following the second new infection, but one of them had meanwhile spent a day with three other febrile women in a four bed ward. On that day the three other women were negative for the streptococcus. Two days later, however, two of them and a third woman in the main ward yielded the same type of streptococcus. The authors believe that in this instance the infection was spread via the air because (1) the noses and throats of the nursing staff yielded no group A streptococci, nor was there any common attendant for all these patients; (2) the spread of infection by hands, instruments or utensils was not probable because of the precautions taken; (3) the infecting type of streptococcus was recovered from the air of the small ward. Cruickshank and Godber also record another suggestive incident in which one of the nurses in a maternity home who had recently recovered from a sore throat and had yielded a negative throat swab apparently was responsible for initiating the infection. One of her patients came down with puerperal fever and was removed to an isolation hospital. Within ten days two additional postparturient women were infected with the same serologic type in spite of the fact that they had been delivered in different labor rooms, housed in separate wards and were never attended by the infected nurse, who was the only one of the nursing personnel found to be carrying a group A streptococcus. Four days after the nurse was taken off duty because her throat was again positive, two additional attendants contracted tonsillitis, caused by the same serologic type. It should be added that all the nurses wore masks while on duty.

These findings indicate a possible role for air borne infection in maternity wards, in line with the clinical opinions of De Lee [40] and of Leonard Colebrook [31] as well as of Robinson and Cuttle [41] on puerperal scarlet fever. The evidence, nevertheless, is not so strong as that which might be obtained by more extensive bacteriologic investigation.

Children's Hospitals: Nosocomial respiratory infections in infants' and children's hospitals constitute another serious problem. Although no extended and detailed study of air as a vehicle of contagion in these hospitals has been made, the types of infections that do occur suggest a mechanism or mechanisms similar to those found in other wards. Long and his associates [42] in the Infants' Hospital, Boston, found in one year an incidence of 12.6 per cent (185 of 1,445) of new infections, of which 7.1 per cent (110) were respiratory, and in a second year an incidence of infection of 10.3 per cent (60 of 585), of which 6.5 per cent (38) were respiratory. It is of interest that these relatively high rates occurred despite the fact that all the children were nursed in cubicles (without doors). In some instances the possible primary source of infection could be traced to a nurse or other patient, but in others it could not be traced. The Boston workers were of the opinion that masking of the personnel was efficacious in reducing the incidence of infection. However, Wright [43] of the University College Hospital, London, came to the conclusion that the upper respiratory tract of nurses did not seem to play an important part in the spread of infection among children in that institution. She found a higher intercurrent infection rate, 18.9 per cent (104 of 551), than did the Boston workers and also determined that streptococci were acquired by 13.1 per cent (72) of the children during hospitalization. Wright studied four different outbreaks of streptococcic infections, each of which was caused by a specific serologic type. Although in some instances the infection seemed to spread from bed to bed, she concluded that the exact mode of spread was not ascertainable. Lately Coburn

35. Congdon, P. M.: Streptococcal Infection in Childbirth and Septic Abortion: Source of Infection and Grouping of Hemolytic Strains, Lancet **2**: 1287 (Dec. 7) 1935.

36. Hare, Ronald, and Colebrook, Leonard: Biochemical Reactions of Hemolytic Streptococci from Vagina of Febrile and Afebrile Parturient Women, J. Path. & Bact. **39**: 429 (Sept.) 1934.

37. Bryce, L. M., and Tewsley, P.: A Bacteriological and Clinical Study of the Professional Personnel of Maternity Hospitals with Special Reference to Carriers of Hemolytic Streptococci, M. J. Australia **1**: 639 (April 9) 1938. Bryce, L. M.: Note on Type of Haemolytic Streptococci Occurring in Outbreak of Puerperal Sepsis, ibid. **1**: 900 (June 17) 1939.

38. White, Elizabeth: On the Possible Transmission of Haemolytic Streptococci by Dust, Lancet **1**: 941 (April 25) 1936.

39. Cruickshank, R., and Godber, G. E.: The Aerial Spread of Streptococcal Infections, Lancet **1**: 741 (April 1) 1939.

40. De Lee, J. B., and Siedentopf, Heinz: The Maternity Ward of the General Hospital, J. A. M. A. **100**: 6 (Jan. 7) 1933.

41. Robinson, A. L., and Cuttle G. E.: Infectious Puerperal Fever, Lancet **1**: 67 (Jan. 11) 1930.

42. Long, A. P.; McKhann, C. F., and Cheney, L. L.: Hospital Infections: II. Nasopharyngeal Flora and Disease of the Respiratory Tract in Infants, Am. J. Dis. Child. **57**: 1363 (June) 1939; III. A Ward Study for Sources of Infection, ibid. **60**: 322 (Aug.) 1940.

43. Wright, Joyce: Nosocomial Infections in Children's Wards, J. Hyg. **40**: 647 (Dec.) 1940.

and Pauli [44] have reported a fairly extensive streptococcus epidemic in Babies Hospital in New York which they believe to have been dust borne.

Other Hospitals: The possibility of air borne spread of streptococcic infections in other hospital departments is suggested by a number of studies. Thus, in a ward where burns were treated Cruickshank [45] found that the incidence of streptococcic infections in burns increased from 11 per cent (11 of 100) on admission to 51 per cent after periods of time ranging up to two months.[46] Cruickshank was also able to recover many streptococci from the air of this ward. Likewise, streptococcic infections occurring in operating rooms have been traced to the nasopharynx of nurses by Meleney and Stevens,[47] and by Miles and his associates.[48] Similarly in studies in otorhinologic wards Okell and Elliot,[28] supported by Garrod,[49] have traced cross infections which suggested an air borne basis to them, and Keevil and Camps [50] were able to recover streptococci of the same type as those found among the patients from the air of a general hospital ward and a maternity ward.

A problem of the hour is the infection of war wounds during hospitalization. In the first world war Fleming and Porteus [51] found that, while the wounds of 20 per cent of patients were infected with streptococci on reaching a base hospital, those of 90 per cent were thus infected after one week's stay. Stokes and Tyler [52] reported similar findings. Hare [53] has suggested that the relatively high rate of infection on admission is explainable by the gantlet of hands and throats through which the patient must travel before entering the base hospital—hands and throat with streptococcus carrier rates of 0 to 4 per cent and about 7 per cent respectively (Colebrook, Maxted and Johns; [54] Hare [55]). The findings in the current war are similar. Miles and his associates [48] report that the organisms most frequently found in wounds on admission to the hospital are hemolytic staphylococci and streptococci and that the wounds of 58 per cent (43) of a group of 74 patients acquired a new species of bacteria in an average time of about ten days after admission. As has been shown in other wards during peace time, the spread of streptococci to wounds can be traced by serologic typing. It is interesting to note that twenty of twenty-nine wounds treated with plaster casts yielded streptococci and that clinical signs of infection were manifested by about 80 per cent of those infected. These authors and Hare and Willits,[55] who were able to recover from the ward air the infecting streptococci of 9 of 11 patients, suggest that hospital dust is an important source of infection and their position is supported editorially by the *Lancet* [56] as follows: "There is still a certain reluctance to accept air borne bacteria as a factor in hospital cross infection, partly because of the apparent paucity of pathogens in the air of the ward, partly because bacteria in air or dust are regarded as less likely to be in an active vegetative state than those coming directly from the body tissues, yet it seems likely that a very few streptococci will be sufficient to initiate infection on an abraded surface, and there is increasing evidence that the air and dust of the ward are the vehicles for the spread of infection." Incidentally the possibility of the indirect spread of infection by stirred up dust rather than by droplets, or the so-called droplet nuclei of Wells, is supported by an observation of Hare's.[57] He recovered streptococci from the rooms of two of five students who had suffered from upper respiratory infections. In one instance a student had been confined to his room for three or four days with streptococcic sore throat and a paronychia. The specific serologic type was recovered from the bed sheets, pillow, pajamas and carpet. Three weeks later, with the student still carrying the organisms, it was again recovered from his bed sheet and pajamas. Incidentally Hare [58] came to a similar conclusion on the relative importance of dust as the result of a laboratory investigation. He could find little evidence for the expulsion of droplet nuclei by normal carriers of hemolytic streptococci during talking or even coughing. It is only fair to add, however, that the possible expulsion of droplet nuclei during sneezing by healthy or sick carriers was not investigated.

PNEUMOCOCCIC INFECTIONS

Pneumonia is now recognized to be a contagious disease. This is because (1) epidemics due to specific types of pneumonia sometimes occur in children's institutions, men's dormitories, hospitals for the insane and isolated villages,[59] (2) 2 or more cases caused by the same strain sometimes occur within a small time interval in the same family or in a hospital ward [60] and (3) immediate contacts in families and in hospitals sometimes yield a greater proportion of throat carriers of

44. Coburn, A. F., and Pauli, R. H.: The Interaction of Host and Bacterium in the Development of Communicability by Streptococcus Hemolyticus, J. Exper. Med. **73**: 551 (April) 1941.

45. Cruickshank, Robert: The Bacterial Infection of Burns, J. Path. & Bact. **41**: 367 (Sept.) 1935.

46. It has been suggested that the toxic effect of burns is caused by bacterial infection. (Aldrich, R. H.: The Role of Infection in Burns, New England J. Med. **208**: 299 [Feb. 9] 1933.)

47. Meleney, F. L., and Stevens, F. A.: Postoperative Hemolytic Streptococcus Wound Infections and Their Relation to Hemolytic Streptococcus Carriers Among the Operating Personnel, Surg., Gynec. & Obst. **43**: 338 (Sept.) 1926.

48. Miles, A. A.; Schwabacher, H.; Cunliffe, A. C.; Ross, J. P.; Spooner, E. T. C.; Pilcher, R. S., and Wright, J.: Hospital Infection of War Wounds, Brit. M. J. **2**: 855 (Dec. 28) 1940.

49. Garrod, T. P.: Cross Infections in Otorhinological Wards, Lancet **2**: 944 (Oct. 17) 1936.

50. Keevil, N. L., and Camps, F. E.: Epidemic Streptococcal Infections in a General Hospital, Lancet **2**: 207 (July 24) 1937.

51. Fleming, A., and Porteus, A. B.: Streptococcal Infections of Septic Wounds at a Base Hospital, Lancet **2**: 49 (July 12) 1919.

52. Stokes, A., and Tyler, W. H.: Bacteriology of Wounds, Brit. J. Surg. **6**: 92 (July) 1918.

53. Hare, Ronald: Sources of Haemolytic Streptococcal Infection of Wounds in War and in Civil Life, Lancet **1**: 109 (Jan. 20) 1940.

54. Colebrook, Leonard; Maxted, W. R., and Johns, A. M.: Presence of Haemolytic and Other Streptococci on Human Skin, J. Path. & Bact. **41**: 521 (Nov.) 1935.

55. Hare, Ronald, and Willits, R. E.: The Source and Prevention of Septic Infection of Wounds, Canad. M. A. J. **44**: 230 (March) 1941.

56. Cross Infection of Wounds, editorial, Lancet **1**: 79 (Jan. 18) 1941.

57. Hare, Ronald: Hemolytic Streptococci in Normal People and Carriers, Lancet **1**: 85 (Jan. 18) 1941.

58. Hare, Ronald: The Expulsion of Hemolytic Streptococci by Nasopharyngeal Carriers, Canad. Pub. Health J. **31**: 539 (Nov.) 1940.

59. Schroder, M. C., and Cooper, G.: An Epidemic of Colds, Bronchitis and Pneumonia Due to Type V Pneumococci, J. Infect. Dis. **46**: 384 (May) 1930. Strøm, A.: An Epidemic of Croupous Pneumonia Caused by Pneumococcus Type I, ibid. **50**: 430 (May-June) 1932. Wallbruch, E.: Die lobare Pneumonie als epidemisch auftretende Erkrankung, Ztschr. f. Hyg. u. Infektionskr. **117**: 92, 1935. Smillie, W. G.: A Study of an Outbreak of Type II Pneumococcic Pneumonia in the Veterans' Administration Hospital at Bedford, Mass, Am. J. Hyg. **24**: 522 (Nov.) 1936. Harris, A. H., Jr., and Ingraham, H. S.: A Study of the Carrier Condition Associated with Type II Pneumonia in a Camp of the Civilian Conservation Corps, J. Clin. Investigation **16**: 41 (Jan.) 1937. Gilman, B. B., and Anderson, G. W.: A Community Outbreak of Type I Pneumococcic Infection, Am. J. Hyg. **28**: 345 (Nov.) 1938. Smillie, W. G.; Warnock, G. H., and White, H. J.: A Study of the Type I Epidemic at the State Hospital at Worcester, Mass., Am. J. Pub. Health **28**: 293 (March) 1938. Benjamin, J. E.; Ruegsegger, J. M., and Senior, F. A.: Cross Infection in Pneumococcic Pneumonia, J. A. M. A. **112**: 1127 (March 25) 1939. Stebbins, E. L.; Perkins, J. E.; Rogers, E. S.; Champlin, R. D., and Ames, W. R.: Prevalence of Pneumococcus Carriers; Specific Types in Epidemic and Nonepidemic Areas, Am. J. Pub. Health **30**: 349 (April) 1940. Dauer, C. C.; Dowling, H. F., and Noble, J. E.: An Outbreak of Type II Pneumococcus Pneumonia in an Institution for Children, Am. J. Hyg., Sect. A **33**: 1 (Jan.) 1941.

60. Tilghman, R. C., and Finland, Maxwell: Pneumococcic Infections in Families, J. Clin. Investigation **15**: 493 (Sept.) 1936. Finland, Maxwell, and Tilghman, R. C.: Bacteriological and Immunological Studies in Families with Pneumococcic Infections: The Development of Type-Specific Antibodies in Healthy Contact Carriers, ibid. **15**: 501 (Sept.) 1936. Benjamin, Ruegsegger and Senior.[59] Holle, H. A., and Bullowa, J. G. M.: Pneumococcal Cross Infections in the Home and Hospital, New England J. Med. **223**: 887 (Nov. 28) 1940. Rogers, E. S.; Robins, M., and Arnstein, M. G.: Secondary Attack Rates in Pneumonia, Am. J. Pub. Health **31**: 135 (Feb.) 1941.

the specific type than is found in the population at large.[61]

Although the biology of the pneumococcus is in some respects similar to that of the streptococcus, little direct evidence has been adduced for the air borne transmission of pneumococcic infection. This may or may not be due to the fact that the possibility of air borne infection has not been extensively investigated. The only clinical evidence for the air borne route of infection is that pneumococci apparently can be recovered from the environment of patients without great difficulty. In the early years of bacteriology there were several reports that pneumococci could be recovered from house and hospital dust (Netter; Maximovitsch; Emmerich; Washbourn and Eyre, all cited by Washbourn[62]), and in 1917 Stillman[63] was able to recover pneumococci frequently enough from house dust to write that "the occurrence of these disease producing types of pneumococci in the dust suggests the possibility that air borne infection may play a part in the production of pneumonia." Stillman had been able to isolate pneumococci of the homologous type from the floor dust of the homes of 50 per cent (26 of 52) of patients with pneumonia caused by types I or II who were admitted to the hospital of the Rockefeller Institute. It is of interest that contacts in only 28 per cent (15 of 52) of these homes yielded throat cultures of the homologous type of pneumococcus.

DIPHTHERITIC INFECTIONS

It has been pointed out both by Kemkes and Steigler[64] and by Glass and Wright[65] that some hospitalized diphtheria patients suffer reinfections by diphtheria bacilli. Wright, Shone and Tucker,[66] who investigated the incidence of such infections and their mode of spread, concluded that ". . . contact between patients is responsible in large part for cross infection but that other important sources are carriers among the ward staff and the dust on the floor of the ward." The data presented are of the same type as those obtained in scarlet fever wards. It seems however that, although the existence of air borne infection is definitely appreciated by these authors, its extent may not be. Thus they express discouragement because the incidence of reinfection was not very much lower in two wards nursed by bed isolation (5 per cent) than in two others not so nursed (10 per cent). Furthermore, their data indicate that the number of reinfections found is probably much less than the number which actually occurred. Thus they noted that only 4 of 33 patients who were originally infected with the gravis type became reinfected, whereas 5 of 16 originally infected with either the intermedius or the mitis type were so afflicted. This difference in the percentage incidence of reinfection can probably be ascribed to the fact that in order that a new infection be recognized it must be induced by one of the two types not causing the original infection. Two thirds of the patients, however, were infected by the gravis type and so reinfections which might be caused by this type would have been largely undetectable. These patients, accordingly, would be susceptible to apparent reinfection only by strains from the remaining third of the patients. The latter, on the other hand, were susceptible to demonstrable reinfection for more than two thirds of the other patients. The authors believe that nurse contacts may be important in the spread of infection, but only 12 nurses of 122, from whom 714 pairs of swabs were taken, were found to be positive for the diphtheria bacillus and in one ward 33 nurses from whom 193 pairs of swabs were taken, were all negative. Furthermore, it was found that a number of patients nursed in cubicles for fairly extended periods showed no signs of reinfection, which is not what would be expected if nurses play an important role in the dissemination of infection. Finally they were able to recover diphtheria bacilli from the floor sweepings of four wards in one hospital in sixteen of seventeen trials, from two of three wards in a second hospital and from three of four wards in a third hospital. As might be expected from the previous information, gravis was the predominant type recovered. In some instances the number of colonies recovered was small, but more often it was large, and in many instances several hundred were present on each plate. Three samples of dust which were kept in test tubes and reexamined after a month yielded about the same numbers of still virulent organisms. In one specimen a gravis strain remained alive and virulent for two months. These facts appear to have had sufficient appreciation by the authors to justify their making the following statement: "We have been surprised at the ease and frequency with which Corynebacterium diphtheriae can be demonstrated in ward sweepings and at times astounded at the enormous numbers of fully virulent gravis organisms which appear on plates."

THE "THERAPEUTIC TEST" OF THE AIR BORNE HYPOTHESIS

What might be called a therapeutic test of the air borne hypothesis has been carried on during the past several years. If the air borne route is important, measures which rid the environment of micro-organisms which might spread by this means should reduce the incidence of respiratory infections. This has actually been found in several instances in work which is still in its earliest phases.

Before the methods used and the results obtained are discussed, however, it may be of value to construct an ideal picture of the distribution of micro-organisms in a sickroom. If we could actually see the streptococci in a scarlet fever ward the following is what we might observe: Entering about 9 o'clock in the morning we examine 1 of the patients. Many streptococci are seen in his nose and throat. Smaller numbers are also observed on his hands; a few are noted on his face in the region of the nose and mouth, and an occasional one appears on more distant surfaces. Likewise the nasopharynx of an attendant is seen to harbor the same type of organism but not in such large numbers; some streptococci are noted on her hands and several on her clothes as well. Examination of the bed reveals a fair number of organisms resting on the top sheet. When this is lifted off others are seen on the undersheets, the pillows and the bedclothes of the patient. A glance at the air of the room next reveals a fairly uniform distribution of streptococci, except for a temporary concentration within a radius of a few yards of a patient who has just sneezed and around a bed the linen of which is being changed. It is also noted that strepto-

61. There have been many confirmations of this finding, first reported by Dochez, and Avery: (The Occurrence of Carriers of Disease Producing Types of Pneumococcus, J. Exper. Med. **22**: 105, 1915).

62. Washbourn, J. W.: The Natural History and Pathology of Pneumonia, Lancet **2**: 1439, 1902.

63. Stillman, E. G.: Further Studies on the Epidemiology of Lobar Pneumonia, J. Exper. Med. **26**: 513 (Oct.) 1917.

64. Kemkes, B., and Steigler, A.: Zur Typenverteilung der Diphtheriebacillen und zur Frage der Superinfektion in Krankenanstalten, Klin. Wchnschr. **16**: 1649 (Nov. 20) 1937.

65. Glass, V., and Wright, H. D.: Cross Infection in Diphtheria Wards, J. Hyg. **38**: 248 (March) 1938.

66. Wright, H. D.; Shone, H. R., and Tucker, J. R.: Cross Infection in Diphtheria Wards, J. Path. & Bact. **52**: 111 (Jan.) 1941.

cocci are settling out on the floor in a regular manner. Further study of the floor reveals many organisms which tend to gather near the beds and diminish in number around the windows, particularly at the southern end of the room. At this point an attendant walks briskly through the room with his long coat fluttering in the breeze, and it is noted that many streptococci are stirred up from the floor and become resuspended in the air. Finally, if we were to return to the ward in the middle of the night we might observe few organisms in the air but many on the floor.

It is clear then that any ideal system which may be developed for the prevention of air borne transmission of streptococcic infection in a scarlet fever ward must destroy the organisms situated in the following places:

A. The host:

1. The patient's nasopharynx, hands and bedclothes.
2. His attendant's nasopharynx and perhaps his hands and clothes as well.

B. The environment:

1. The air of the room.
2. The floor of the room.

It is obvious that no single method so far advocated can be expected to eliminate streptococci from all these areas. For practical purposes, however, two distinct lines of approach are possible, each of which attempts to break the infection cycle at a different point:

The first would attempt to destroy micro-organisms at their immediate source, i. e. in the host, or to prevent the throats of others from becoming infected. This is technically the most difficult procedure and but little effort has been expended on it until very recently. Delafield, Straker and Topley[67] (1941) have reported that the use of snuffs made of sulfathiazole, penicillin or proflavine, with a base of lycopodium spores or magnesium carbonate, temporarily reduced the number of organisms recoverable from the nose of staphylococcus carriers. Similarly Young and Charteris[68] suggest that sprays of proflavine and acriflavine cut down the incidence of postoperative scarlet fever in a nose and throat department.

The second approach, for which the air borne hypothesis serves as a rationale, is to attempt to rid the environment of its micro-organisms. At present two main lines are being followed toward this end, although several subsidiary ones have been suggested. One of these attempts to destroy the micro-organisms by ultraviolet light and the other by chemical sprays, the so-called aerosols.

ULTRAVIOLET LIGHT

Up to the present ultraviolet light has been the most widely used of the two, largely because of the pioneering efforts of Wells.[69] Lamps emitting these rays are now installed in infants' and children's hospitals, in nursing homes for children, in operating rooms and in schools. Such lamps are highly bactericidal; it is asserted by Wells that micro-organisms can be removed from air by this means at a rate far greater than that attainable by any type of mechanical ventilation. Furthermore the method has the advantage that it is almost automatic in operation. There are two minor limitations to the use of ultraviolet light which are, however, far from insurmountable. The first is the deleterious effect of ultraviolet light on the eyes and skin. This can be overcome by shielding the body, which is not always feasible, or by shielding the lamp, which may reduce its efficiency. The second objection depends on the inverse square law; lamps suspended from a ceiling are least effective against bacteria which are on the floor.

The use of ultraviolet light has yielded encouraging results despite the fact that the field is only currently being developed.[70] Three reports have appeared concerning the disease chickenpox, which is presumably of virus causation and about whose mode of transmission little is known. McKhann and his associates[71] reported that chickenpox failed to spread from 12 cases treated in an isolation ward over a period of five months to all but 1 of 120 other children on the same floor who were separated from the infected room by an ultraviolet light barrier. Greene and his associates[72] reported a still more striking result. They were engaged in a study of the effectiveness of ultraviolet light in a home for infants and children when an epidemic of chickenpox occurred. At that time they had under study two infants' wards, one with and the other without ultraviolet light. Ninety-seven per cent (165 of 170) of the children who were housed in the main building and 18 of 19 in the unirradiated control ward contracted chickenpox, whereas in the irradiated ward not a single case developed. It is interesting that a night nurse in the latter ward also cared for children in an adjoining ward, where the incidence of infection was 100 per cent. Finally, Wells[73] has reported that for three successive years young children in the irradiated rooms of a school were spared not only from chickenpox but from mumps as well, when these diseases were prevalent in other parts of the school.

There have also been two reports on the effectiveness of ultraviolet light in reducing the general incidence of respiratory infections as a whole in children's institutions. Encouraging results have been published by del Mundo and McKhann,[74] who used ultraviolet barriers across the entrance of the individual cubicles in an infants' hospital, and by Greene and his associates in the study mentioned.

The first practical results of the use of ultraviolet light in operating rooms were reported by Hart,[75]

67. Delafield, M. E.; Straker, E., and Topley, W. W. C.: Antiseptic Snuffs, Brit. M. J. **1:** 145 (Feb. 1) 1941.

68. Young, G., and Charteris, A. A.: Use of Proflavine and Acriflavine in a Throat and Nose Department, Brit. M. J. **2:** 489 (Oct. 12) 1940.

69. Wells, W. F., and Fair, G. M.: Viability of B. Coli Exposed to Ultraviolet Radiation in Air, Science **82:** 280 (Sept. 20) 1935. Wells, W. F., and Wells, Mildred W.: Air Borne Infection, J. A. M. A. **107:** 1698 (Nov. 21), 1805 (Nov. 28) 1936. Sharp, D. G.: A Quantitative Method of Determining the Lethal Effect of Ultraviolet Light on Bacteria Suspended in Air, J. Bact. **35:** 589 (June) 1938. Koller, L. R.: Bactericidal Effects of Ultraviolet Radiation Produced by Low Pressure Mercury Vapor Lamps, J. Appl. Physiol. **10:** 624, 1939. Wells, W. F., and Wells, Mildred W.: Measurement of Sanitary Ventilation, Am. J. Pub. Health **28:** 343 (March) 1938. Wells, W. F.; Wells, Mildred W., and Mudd, Stuart: Infection of Air: Bacteriologic and Epidemiologic Factors, ibid. **29:** 863 (Aug.) 1939. Wells, W. F.: Bactericidal Irradiation of Air: Part I. Physical Factors, J. Franklin Inst. **220:** 347, 1940.

70. Wells, W. F.; Stokes, J., Jr.; Wells, Mildred W., and Wilder, T. S.: Experiments in the Environmental Control of Epidemic Respiratory Infection, Tr. & Stud., Coll. Physicians, Philadelphia **7:** 342, 1940. Robertson, E. C.; Doyle, M. E.; Tisdale, F. F.; Koller, L. R., and Ward, F. S.: Air Contamination and Air Sterilization, Am. J. Dis. Child. **58:** 1023 (Nov.) 1939.

71. McKhann, C. F.; Steeger, A., and Long, A. P.: Hospital Infections: I. A Survey of the Problem, Am. J. Dis. Child. **55:** 579 (March) 1938.

72. Greene, David; Barenberg, L. H., and Greenberg, Bernard: Effect of Irradiation of the Air in a Ward on the Incidence of Infections of the Respiratory Tract with a Note on Varicella, Am. J. Dis. Child. **61:** 273 (Feb.) 1941.

73. Wells, W. F.: Studies on Air Borne Infection, Science **92:** 457 (Nov. 15) 1940.

74. del Mundo, F., and McKhann, C. F.: Effect of Ultraviolet Radiation of Air on Incidence of Infections in an Infants' Hospital, Am. J. Dis. Child. **61:** 213 (Feb.) 1941.

75. Hart, Deryl: Sterilization of the Air in Operating Room by Special Bactericidal Radiant Energy: Results of Its Use in Extrapleural Thoracoplasties, J. Thoracic Surg. **6:** 45 (Oct.) 1936. Hart, Deryl, and Gardner, C. E., Jr.: Sterilization of the Air in the Operative Region with Bactericidal Radiant Energy, Tr. South. S. A. **49:** 377, 1937. Hart, Deryl, and Schiebel, H. M.: Role of Respiratory Tract in Contamination of Air, Arch. Surg. **38:** 788 (April) 1939. Hart, Deryl: Sterilization of Air in Operating Room with Bactericidal Radiation: Results from Nov. 1, 1938 to Nov. 1, 1939, with Further Report as to Safety of Patients and Personnel, ibid. **41:** 334 (Aug.) 1940.

who, with his associates, has found that infections with Staphylococcus aureus after thoracoplasty were definitely reduced by this means. There is now little or no question that ultraviolet light reduces the number of organisms in the air of operating rooms (Robertson and Doyle [76]) as well as the incidence of wound infections after several different types of operation (Meleney [77]). However, it has been pointed out that wounds may also be contaminated directly by skin carriers of Staphylococcus aureus. Thus Gillespie, Devenish and Cowan [78] noted a significant skin (wrist) carrier rate of that organism, and Devenish and Miles [79] found that the high incidence of infection in one operating room could be traced to a surgeon who was such a carrier. They believed that infected sweat, leaking through gloves, which were often punctured, was responsible for most of the infections.

It is noteworthy that a subcommittee of the Council on Hospital Planning and Plant Operation of the American Hospital Association has recommended that the installation of ultraviolet light equipment should be considered when new contagious disease or surgical operating units are built.[80]

CHEMICAL SPRAYS

It is many years since the practice of spraying phenol (carbolic acid) into the air of operating rooms, introduced by Lister, was abandoned. Aseptic technic had come to be considered sufficient to prevent infection during operations. With the rebirth of the air borne hypothesis the general method of spraying germicidal agents into the air has been revived, although now a much wider application is intended (Trillat and Fouassier [81]).

Chemical sprays possess a theoretical advantage over ultraviolet light in that they may have greater penetrating power and be more effective at a distance. Sprays, however, may be noxious or unpleasant to man or injurious to room furnishings, and, unlike ultraviolet light, their application must be constantly supervised. At present the ability of three groups of substances to kill bacteria suspended in air is being studied: (1) sodium hypochlorite, (2) substances of known disinfecting power such as resorcinol and hexylresorcinol dissolved in a vehicle such as propylene glycol and (3) some of the higher alcohols alone, such as propylene glycol, ethylene glycol and trimethylene glycol. Most of the substances of all three groups which have been tested by spraying have been found to be potent germicides for bacteria suspended in air.

The first germicidal spray advocated in the present era was sodium hypochlorite. Douglas, Hill and Smith [82] in 1928 reported that this substance would produce a great reduction in the number of organisms in the air of a room previously sprayed with Escherichia coli. In 1938 Masterman [83] confirmed the efficacy of hypochlorite when sprayed in dilute solution in a normal room environment and promoted an apparatus for its practical application. In the same year Trillat [84] also pointed out the possible usefulness of sodium hypochlorite. Some difference of opinion exists, however, as to the mode of action of sodium hypochlorite and its relative worth as a practical aerosol. Baker, Finn and Twort [85] believe that hypochlorous acid is more lethal when in solution and sprayed as a mist than when used in gaseous form and also suggest that its use is limited by its odor, irritating effects and opacity. Masterman [86] disagrees. He is of the opinion that gaseous hypochlorous acid is the most effective phase of the germicide and that its objectionable qualities are more theoretical than actual. Likewise Pulvertaft and Walker [87] believe that the cheapness and deodorizing qualities of the hypochlorite compensates to some extent for its lesser effectiveness as compared with some other substances.

In 1938 Trillat [84] advocated the use of a supersaturated aqueous solution of resorcinol with glycerin and suggested that the germicidal efficiency of chemical substances was dependent on the interaction of very small particles of the incompletely evaporated mist with the suspended bacteria. Pulvertaft, Lemon and Walker [88] confirmed his finding and also noted the effectiveness of a solution of 5 per cent chloramine-T in acetone, alcohol, glycerin and water to which a small amount of sulfonated oleic acid had been added as a wetting agent. They observed that this mixture was efficiently bactericidal only when the infectious material was allowed to dry. They also reported that bacteria on a porous test surface, in contrast to those on a smooth surface, were not very efficiently attacked by any of the germicides tested except solution of formaldehyde. Pulvertaft and Walker [87] later devised a solution in which resorcinol replaced chloramine-T, and ethylene glycol replaced glycerin.

The most comprehensive single study on chemical sprays up to the present is that of Twort, Baker, Finn and Powell.[89] These workers found that, although many substances exerted a germicidal effect in the air, the extent of which could not be predicted from their in vitro activity, the most effective all around solution was one in which 10 per cent hexylresorcinol was dissolved in propylene glycol to which was added 0.05 per cent sulfonated lauryl. They came to the conclusion that the most effective germicidal particles were those of a radius of 0.5 to 1.0 micron. They also found that germicidal mists were capable of penetrating cloth barriers and acting on bacteria within and that, though the mists were relatively effective in killing bacteria on horizontal smooth surfaces, they were less effective on vertical ones.

76. Robertson, E. C., and Doyle, M. E.: On Control of Air Borne Bacteria in Operating Rooms and Hospital Wards, Ann. Surg. **111:** 491 (March) 1940.

77. Meleney, F. L.: The Prevention and Treatment of Infection in Wounds, Both Operative and Accidental, Bull. New York Acad. Med. **17:** 221 (March) 1941.

78. Gillespie, E. H.; Devenish, E. A., and Cowan, S. T.: Pathogenic Staphylococci. Their Incidence in the Nose and on the Skin, Lancet **2:** 870 (Oct. 21) 1939.

79. Devenish, E. A., and Miles, A. A.: Control of Staphylococcus Aureus in an Operating Theater, Lancet **1:** 1088 (May 13) 1939.

80. Ultraviolet Rays as a Sterilization Agent in Hospitals, Council on Hospital Planning and Plant Operation, Am. Hosp. A. Bull., 1940, no. 203.

81. Trillat, A., and Fouassier, M.: Action des doses infinitésimales de diverses substances alcalines fixes ou volatiles sur la vitalité des microbes, Compt. rend. Acad. d. sc. **155:** 1184, 1912; Influence de la radio-activité de l'air sur les goutelettes microbiennes de l'atmosphère, ibid. **159:** 817, 1914.

82. Douglas, S. R.; Hill, L., and Smith, W.: Effect of Antiseptic Sprays on the Bacterial Content of Air, J. Indust. Hyg. **10:** 219, 1928.

83. Masterman, A. T.: Air Purification in Inhabited Rooms by Spraying or Atomizing Hypochlorites, J. Indust. Hyg. & Toxicol. **40:** 278 (April) 1938.

84. Trillat, A.: Propriété des aérosols microbiens: applications, Ann. d'hyg. **16:** 49 (Feb.) 1938; Sur la désinfection dite "permanente," Hyg. sociale **7:** 178, 1938. Les aérosols microbiens: applications, Bull. Acad. de méd., Paris **119:** 64 (Jan. 11) 1938.

85. Baker, A. H.; Finn, S. R., and Twort, C. C.: The Use of Hypochlorites for Aerial Disinfection, J. Hyg. **40:** 560 (Sept.) 1940.

86. Masterman, A. T.: Air Purification by Hypochlorous Acid Gas, J. Hyg. **41:** 44 (Jan.) 1941.

87. Pulvertaft, R. J. V., and Walker, J. W.: The Control of Air Borne Bacteria and Fungus Spores by Means of Aerosols, J. Hyg. **39:** 696 (Nov.) 1939.

88. Pulvertaft, R. J. V.; Lemon, G. C., and Walker, J. W.: Atmospheric and Surface Sterilization by Aerosols, Lancet **1:** 443 (Feb. 25) 1939.

89. Twort, C. C.; Baker, A. H.; Finn, S. R., and Powell, E. O.: The Disinfection of Closed Atmospheres with Germicidal Aerosols, J. Hyg. **40:** 253 (May) 1940.

Twort and his associates believe that the solvent plays a more significant role in the action of aerial germicides than has been considered and state that they were investigating the potency of glycol solutions when used alone. Meanwhile a report by Robertson and his co-workers [90] indicates that propylene glycol, ethylene glycol and trimethylene glycol are all effective aerial germicides. Twort and Baker [91] have reported on the germicidal activity of several organic smokes, such as those from cardboard, incense and balsam candles. In a review of the findings of his group Twort [92] has listed the following materials according to a decreasing order of effectiveness; the hexylresorcinol solution described, a supersaturated aqueous solution of resorcinol in glycerin, organic smokes and, lastly, sodium hypochlorite solution. Because of the present emergency in England a group of workers at the National Institute for Medical Research is now investigating the problem.

The possible injurious effects of aerosols generally on experimental animals over long periods has not as yet been adequately studied. Such studies would appear desirable before large scale applications are attempted. Few applications have been reported as yet.

Of two brief notes one, which is nonclinical, records a significant reduction in the number of flasks contaminated in a vaccine bottling laboratory after the air had been sprayed with resorcinol solution (Wats and Kamat [93]). In the other, by Cruickshank and Muir,[94] it is suggested that a resorcinol solution sprayed on two consecutive days into the air of a small ward in which streptococci were widespread immediately reduced the incidence of nose carriers of streptococci from four persons to one. Finally it is noteworthy that sprays are now being used in some air raid shelters in London.[95]

OTHER CONTROL MEASURES

The complete isolation of each bed seems to be the ideal means for combating the aerial spread of infection in hospitals. In default of this procedure the two measures just discussed and others which may be called "common sense" means are indicated. The latter are mechanical ventilation and filtration, which have been shown to limit the bacterial contamination of air in infant incubators (Chapple and Kenny [96]) and the limitation of dust. Most bacteria cast into air must eventually settle on some surface. When that surface happens to be a floor or a bed, some of the bacteria will inevitably be resuspended in the air. A practical method of preventing the raising of bacteria from floors and bedclothes may go a long way toward solving the problem of air borne infection. Certainly the dry sweeping of floors should be discouraged. Likewise improved methods to prevent dust from rising from floors would be valuable. It is of interest that the problem has been approached from this point of view. Van den Ende, Lush and Edward [97] found that, after a floor had been treated with crude liquid paraffin (spindle oil) and then inoculated with streptococci, few organisms could be raised from the floor by sweeping for one minute. One coating, which was slippery for twenty-four hours, lasted for at least ten days even if treated with soap or saponated solution of cresol. However, these workers were unable effectively to combine an antiseptic with the oil. It is also suggested [98] that bed coverings can be made to retain bacterial dust by treatment with 30 per cent liquid paraffin in white spirit (a petroleum product used in dry cleaning).

SUMMARY

The hypothesis that respiratory infections are largely air borne is considered more satisfactory than the theory that they are spread by direct contact because of the findings along three distinct lines of research.

The first consists of evidence adduced by surveys and laboratory studies. It has been shown that an organism such as the alpha hemolytic streptococcus, which is a common nonpathogenic inhabitant of the upper respiratory tract of man, can be recovered readily from man's environment. This organism can survive for days in indoor environments, and the numbers found in any location seem to serve as an index of the conditions of occupancy and ventilation. Strains of the human pathogenic group A beta hemolytic streptococcus can also be recovered from a "normal" environment with practically unimpaired virulence, although in relatively small numbers. In the laboratory it has been shown that streptococci artificially sneezed into air float for relatively long periods. They settle out geometrically and, having settled, they die geometrically at rates which vary with the length of the bacterial chain and prevailing conditions of the environment. Organisms which have settled out of air may be readily resuspended therein. In the presence of sunlight and even diffuse daylight which have passed through the glass of a window, both streptococci and pneumococci on a simulated floor die at a much faster rate than they do in the dark. If the air borne route is an important vehicle for the spread of respiratory infection, then ordinary diffuse daylight in rooms may act as a strong deterrent to the spread of such infections.

Little is known of the manner of spread of virus infections of the respiratory tract, but it has been shown in the laboratory that ferrets can be infected by spraying the air with influenza virus and that this virus can be recovered from the air after thirty minutes. Likewise when the intact chorioallantoic membrane of the developing chick embryo is exposed to air sprayed with vaccinia virus the virus can be recovered for at least eight hours.

Investigations of hospital infections, particularly those occurring in contagious disease hospitals, have furnished a second group of data supporting the air borne hypothesis. It is now apparent that such infections constitute a serious problem in these institutions as well as in children's, maternity and other hospitals. A long time ago the contact theory seemed to have been confirmed by the success of the so-called barrier method of nursing

90. Robertson, O. H.; Bigg, E.; Miller, B. F., and Baker, Z.: Sterilization of Air by Certain Glycols Employed as Aerosols, Science **93**: 213 (Feb. 28) 1941.

91. Twort, C. C., and Baker, A. H.: Effect of Smoke on Bacteria in the Air, Lancet **2**: 587 (Nov. 9) 1940.

92. Twort, C. C.: Bactericidal Aerosols, Lancet **1**: 61 (Jan. 11) 1941.

93. Wats, R. C., and Kamat, G. K.: The Destruction of Air Borne Bacteria, Indian M. Gaz. **75**: 212 (April) 1940.

94. Cruickshank, R., and Muir, C.: Air Borne Streptococcal Infection Following Influenza, Lancet **1**: 1155 (June 29) 1940.

95. Hygiene in Air Raid Shelters: A Discussion at Meeting of Section of Epidemiology of Royal Society of Medicine, Lancet **1**: 12 (Jan. 4) 1941.

96. Chapple, C. C., and Kenny, A. S.: Limitation of Bacterial Contamination of Air by a New Automatic Incubator for Infants, Am. J. Dis. Child. **57**: 1058 (May) 1939.

97. van den Ende, M.; Lush, D., and Edwards, D. G. F.: Reduction of Dust Borne Bacteria by Treating Floors, Lancet **2**: 133 (Aug. 3) 1940.

98. Andrewes, C. H., and others: Control of Air Borne Infection in Air Raid Shelters and Elsewhere, Lancet **2**: 770 (Dec. 21) 1940.

in contagious disease hospitals, and so it is curious that the best clinical evidence for the air borne hypothesis has now been furnished by institutions of the same kind. In isolation hospitals, particularly, where cross infections due to streptococci and diphtheria bacilli are most prevalent, organisms similar to the causative ones are now known to be present in the air in relatively large numbers and may be presumed to be of practically undiminished virulence. On the whole the data furnished by recent studies on the spread of hospital infections are most satisfactorily explained by the air borne hypothesis.

The third line of evidence has been given by what might be called a therapeutic test of the air borne hypothesis. Measures designed to rid institutional environments of pathogenic micro-organisms should also reduce the incidence of new infections therein. Sufficient laboratory evidence now exists to indicate that ultraviolet light and chemical sprays, the so-called aerosols, may serve as powerful bactericides. The few reports on clinical trials thus far available contain suggestive evidence that in children's hospitals and operating rooms the use of ultraviolet light reduces the incidence of new infections. Furthermore, several reports indicate that the spread of chickenpox in institutions is inhibited by this means. There has been as yet no detailed report on the clinical application of chemical sprays.

Council on Pharmacy and Chemistry

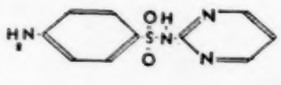
NEW AND NONOFFICIAL REMEDIES

A PRELIMINARY REPORT ON SULFADIAZINE BY THE COUNCIL WAS PUBLISHED IN THE JOURNAL (LONG, PERRIN H.: PRELIMINARY REPORT OF THE COUNCIL, SULFADIAZINE, THE JOURNAL, MAY 24, 1941, PAGE 2399), REVIEWING THE EXPERIMENTAL AND CLINICAL EVIDENCE FOR ITS USE. SINCE THAT TIME OTHER COMMUNICATIONS BY VARIOUS AUTHORS HAVE APPEARED SO THAT THERE NOW EXISTS A MORE COMPLETE KNOWLEDGE OF ITS PHARMACOLOGY AND THERAPEUTIC POSSIBILITIES. PRESENT EVIDENCE INDICATES THAT SULFADIAZINE CAN BE EXPECTED TO GIVE MOST CONSTANT RESULTS IN THE TREATMENT OF INFECTIONS DUE TO DIPLOCOCCUS PNEUMONIAE, HEMOLYTIC STREPTOCOCCUS, MENINGOCOCCIC AND FRIEDLÄNDER'S BACILLUS INFECTIONS, AND STAPHYLOCOCCIC INFECTIONS, GONOCOCCIC INFECTIONS AND URINARY INFECTIONS DUE TO ESCHERICHIA COLI, AEROBACTER AEROGENES, STAPHYLOCOCCI. ITS USE IN OTHER CONDITIONS MUST BE CONSIDERED AS STILL IN THE STAGE OF EXPERIMENTAL INVESTIGATION. AFTER CONSIDERING THE EXISTING EVIDENCE THE COUNCIL VOTED TO ACCEPT SULFADIAZINE FOR INCLUSION IN NEW AND NONOFFICIAL REMEDIES. LEDERLE LABORATORIES, INC., HAS PRESENTED ITS BRAND OF SULFADIAZINE, WHICH THE COUNCIL HAS FOUND TO CONFORM TO ITS OFFICIAL RULES. ACCORDINGLY, THE COUNCIL DECLARED SULFADIAZINE-LEDERLE ACCEPTABLE FOR INCLUSION IN NEW AND NONOFFICIAL REMEDIES.

AUSTIN E. SMITH, M.D., Acting Secretary.

SULFADIAZINE.—2-Sulfanilamidopyrimidine.—2-Sulfanilyl aminopyrimidine.—*p*-amino-N-2-pyrimidyl benzene sulfonamide.—$C_{10}H_{10}N_4O_2S$ (M. W. 250.27).

Sulfadiazine has the following structural formula:



It may be prepared by the reaction of 2-aminopyrimidine with *p*-acetylaminobenzenesulfonyl chloride in the presence of pyridine. The resulting acetylsulfadiazine is hydrolyzed in sodium hydroxide solution, and crude sulfadiazine is obtained by acidifying the mixture with hydrochloric acid. The crude product may be purified by dissolving in alkali, treating with activated charcoal and reprecipitating with hydrochloric acid.

Actions and Uses.—Sulfadiazine is an effective chemotherapeutic agent in the treatment of experimental meningococcic infections, pneumococcic, hemolytic streptococcus, staphylococcic, Friedländer's bacillus, E. Coli, Clostridium septicum and Clostridium welchi infections in mice. Clinically, good therapeutic results have been reported in the treatment of pneumococcic pneumonia, both lobar and bronchial, and hemolytic streptococcus, meningococcic and Friedländer's bacillus infections, also staphylococcic infections, gonococcic infections and urinary infections due to E. coli, A. aerogenes, staphylococci.

Sulfadiazine resembles sulfapyridine more closely in respect to its absorption, distribution and excretion than it does sulfathiazole. When the drug is administered orally, its rate of absorption from the gastrointestinal tract is definitely slower and less complete than that of sulfathiazole or sulfanilamide. Sulfadiazine is, as a rule, conjugated to the acetylated form in the blood and tissues to a lesser degree than is sulfanilamide, sulfathiazole or sulfapyridine. That fraction of the drug which is absorbed is excreted mainly by the kidneys in the "free" and conjugated forms, and it appears that one of the reasons why small amounts of the conjugated fraction are found in the blood is that acetylsulfadiazine is excreted more readily by the kidneys than are the conjugated fractions of sulfapyridine or sulfathiazole. The amount of conjugated drug found in the urine is generally less than that noted in the instance of sulfathiazole or sulfapyridine. The excretion of sulfadiazine is in general slower than that of sulfanilamide, sulfapyridine and sulfathiazole, and it may take five or more days after the drug has been stopped before it is completely eliminated from the body. Probably this slower rate of excretion and the fact that only about 50 per cent of the drug passes into the body water explains why it is possible to obtain and maintain adequate therapeutic levels of sulfadiazine with more ease than is the case when sulfapyridine and sulfathiazole are being prescribed. The drug passes over into pleural and abdominal fluids and into the spinal fluid in concentrations of one half to four fifths of that noted in the blood. Sulfadiazine penetrates the red blood cells easily. It is evident from these findings that the drug is somewhat irregularly distributed in the tissues of the body.

Toxicity.—All observers reporting to date have commented upon the relatively low toxicity of sulfadiazine. Nausea and vomiting are not common, dizziness has occasionally been reported, as have also mild mental disturbances. "Peripheral neuritis" (anterior horn cell injury) has not been noted. Acidosis does not occur. Fever and drug rashes are uncommon, occurring in about 1 or 2 per cent of the patients. Hepatitis has not been reported, leukopenia with granulocytopenia is rare and but 1 case of agranulocytosis (occurring toward the end of the third week of therapy) has been noted. Acute or mild hemolytic anemias are very rare; hematuria and more serious kidney damage are uncommon. Because of the possibility of this latter toxic reaction, it is imperative to keep the urine output of an adult patient receiving this drug at 1,000 cc. a day. If severe toxic manifestations of drug therapy arise, sulfadiazine should be stopped and fluids forced in order that the drug may be eliminated from the body as quickly as possible. It has been noted that patients who are suffering from acute toxic reactions from other drugs in the sulfonamide series may be switched to sulfadiazine therapy without much chance that the existing toxic reaction will be prolonged or accentuated by sulfadiazine. Patients treated with sulfadiazine should be carefully supervised by a physician.

Dosage.—Uniform standards of dosage have not as yet been agreed on by investigators who have used sulfadiazine in the treatment of pneumococcic and other infections. However, it is important to establish adequate concentrations of the drug in the blood as soon as is possible after therapy has been initiated. Hence, in adults with pneumococcic pneumonia, a large initial oral dose is given and should be based on 0.10 Gm. per kilogram, to be followed by doses of 1.0 Gm. of the drug every four hours by mouth until the temperature has been normal for seventy-two hours. The drug may then be stopped. Concentrations of 8 to 12 mg. per hundred cubic centimeters of sulfadiazine in the blood seem advisable during the febrile stage of the pneumonia. In children, the initial oral dose should be based on 0.10 to 0.15 Gm. per kilogram of body weight, and subsequent doses should be one quarter of the initial dose given at intervals of six hours until the temperature has been normal for at least forty-eight hours. In mild or moderate hemolytic streptococcus infections, an initial oral dose of 0.05 Gm. per kilogram, followed by a total daily dose based on 0.10 Gm. per kilogram of body weight, this to be divided into six doses and given every four hours by mouth, day and night, until the temperature has been normal for five days, has been suggested as a satisfactory dosage schedule.

In severe streptococcic and in meningococcic and Friedländer's bacillus infections it is necessary, during the febrile period, to

obtain and maintain concentrations of approximately 15 mg. per hundred cubic centimeters of sulfadiazine in the blood of patients. This can be easily obtained by the intravenous administration of 0.1 Gm. per kilogram of body weight of the sodium salt of sulfadiazine, made up in a 5 per cent solution in sterile distilled water. If the sodium salt has been administered as the initial dose, subsequent doses of the drug should be administered by the oral route and should consist in adults of 1 Gm. every four hours day and night until definite improvement has been noticed. At this time the dosage should be decreased in accordance with the clinical needs of the patient. If the sodium salt of sulfadiazine is not available, the initial oral dose in adults should be, sulfadiazine 0.1 Gm., this to be followed by 1 Gm. every four hours day and night until a definite clinical improvement has been noted. At this time the dose of the drug may be decreased in accordance with the patient's needs. In severe infections in children, the initial oral dose should be based on 0.10 Gm. per kilogram of body weight, and subsequent doses should be one sixth of the initial dose, given at intervals of four hours day and night until definite clinical improvement has been noted; at this time the dose of the drug may be decreased in accordance with the patient's needs. Frequent determinations of the concentration of sulfadiazine in the blood should be made, and this should not be permitted to exceed 20 mg. per hundred cubic centimeters, because higher levels are unnecessary. In mild hemolytic streptococcus infections, in adults, sulfadiazine 1 Gm. every four hours day and night until decided improvement appears is generally sufficient to control the infection.

For the determination of sulfadiazine in body fluids, the method developed by A. C. Bratton and E. K. Marshall Jr. (*J. Biol. Chem.* **128**:537 [May] 1939) is to be recommended.

Sulfadiazine occurs as a white, odorless, tasteless, crystalline powder. It may be recrystallized from hot water to yield long, flat needles which exhibit birefringence, parallel extinction and a negative sign of elongation when viewed under a polarizing microscope. It is soluble in both alkaline and mineral acid solutions; sparingly soluble in alcohol, acetone and water (0.0123 Gm. per hundred cubic centimeters at 37 C.); insoluble in ether and chloroform. The melting point of sulfadiazine is 253-255 C., with decomposition.

Place about 0.5 Gm. of sulfadiazine in a test tube, wrap the upper portion of the test tube with wet filter paper, insert a thermometer and heat at 240-260 C. until a white crystalline sublimate forms in the neck of the tube. The melting point of the crystalline sublimate lies between 120 and 127 C. When recrystallized from hot benzene, the purified 2-aminopyrimidine obtained melts sharply at 126-127 C. (*distinction from other sulfanilamide derivatives*). Under the polarizing microscope the sublimate appears as long, acicular crystals, exhibiting sharp parallel extinction. The fumes evolved during the decomposition do not discolor moistened lead acetate paper (*distinction from sulfathiazole*); no odor of ammonia is evolved, and the residue is colored reddish brown (*distinction from sulfanilamide and sulfaguanidine, which evolve the odor of ammonia and leave a purple to violet residue*).

Dissolve about 0.1 Gm. of sulfadiazine in about 0.5 cc. tenth-normal sodium hydroxide and dilute to 10 cc. with distilled water. Add 5 drops of copper sulfate: an olive green precipitate forms which will change to purple-gray on standing (*distinction from sulfapyridine, which forms an apple green precipitate that turns olive green; from sulfathiazole, which forms a violet precipitate; from sulfaguanidine, which forms a dark brown precipitate; and from sulfanilamide, which forms no precipitate or a light blue one*).

Dissolve 0.5 Gm. of sulfadiazine in a mixture of 5 cc. of nitric acid and 5 cc. of distilled water and add 1 cc. of silver nitrate solution: any turbidity produced is not greater than that formed in a control containing 0.1 cc. of fiftieth-normal hydrochloric acid.

Dissolve 0.5 Gm. of sulfadiazine in 5 cc. of hydrochloric acid and 5 cc. of distilled water and add 1 cc. of barium chloride solution: any turbidity produced is not greater than that formed in a control containing 0.1 cc. of fiftieth-normal sulfuric acid.

Dissolve 1 Gm. of sulfadiazine in 6 cc. of normal sodium hydroxide, dilute to 20 cc. with distilled water, and add 5 drops of freshly prepared 10 per cent sodium sulfide solution: the darkening produced does not exceed that developed in a control test to which has been added 0.02 mg. of lead.

Dry an accurately weighed specimen of sulfadiazine to constant weight in vacuum over phosphorus pentoxide: the loss does not exceed 0.5 per cent.

The nitrogen content of dried sulfadiazine is not less than 22.1 per cent nor more than 22.5 per cent; the sulfur content is not less than 12.5 per cent nor more than 12.9 per cent.

Dissolve about 0.5 Gm. of sulfadiazine in 10 cc. of distilled water and 10 cc. of concentrated hydrochloric acid contained in a 400 cc. beaker, dilute to 50 cc., cool to 15 C., and titrate with tenth-molar sodium nitrite solution.

The endpoint is the first immediate blue streak obtained when a glass rod dipped into the solution is drawn across a smear of starch-iodide paste on white filter paper (or clear glass plate). The solution should retain this endpoint for thirty seconds. Each cubic centimeter of tenth-molar sodium nitrite corresponds to 0.02503 Gm. of anhydrous sulfadiazine: the amount of sulfadiazine found corresponds to not less than 99.5 per cent nor more than 101.0 per cent.

LEDERLE LABORATORIES, INC., PEARL RIVER, N. Y. PATENT APPLIED FOR.

Tablets Sulfadiazine: 0.5 Gm. (7.7 grains).

U. S. patent applied for.

Council on Industrial Health

THIS REPORT ON THE TEACHING OF INDUSTRIAL HEALTH HAS BEEN PREPARED JOINTLY BY COMMITTEES REPRESENTING THE AMERICAN ASSOCIATION OF INDUSTRIAL PHYSICIANS AND SURGEONS AND THE COUNCIL ON INDUSTRIAL HEALTH OF THE AMERICAN MEDICAL ASSOCIATION. THE UNDERLYING ARGUMENTS FOR IMPROVED TEACHING OF THE ESSENTIAL FACTORS IN INDUSTRIAL HEALTH HAVE BEEN SUBMITTED TO THE COUNCIL ON MEDICAL EDUCATION AND HOSPITALS, WHICH IN TURN HAS ACKNOWLEDGED THE URGENT NECESSITY FOR CALLING EXISTING DEFICIENCIES STRONGLY TO THE ATTENTION OF MEDICAL EDUCATORS AND THE PROFESSION AT LARGE AND FOR THE SUBMISSION OF SUITABLE RECOMMENDATIONS AIMED AT THEIR CORRECTION.

C. M. PETERSON, M.D., Secretary.

THE TEACHING OF INDUSTRIAL HEALTH

Recent events have made it plain that the health of the industrial worker is vital to national security. Yet with notable exceptions the requirements of industry in the fields of industrial medicine, surgery and hygiene are being met in very incomplete and fragmentary fashion, without clear realization of objectives or their value to the health status of the community as a whole.[1] It is equally clear that the medical profession has been hampered in its approach to this useful and expanding professional activity and will continue to be hampered until adequate provision is made for instruction in modern industrial health methods, both before and after graduation.

PROFESSIONAL GROUPS INVOLVED

Medical service to industry flows through three principal professional channels:

1. The private practitioner in general or special practice serving on call or part time. Best current estimates indicate that 80 to 85 per cent of medical service to industry is supplied in this fashion. As such it has been mainly remedial in character to such an extent that medium sized and small plants have been left without the considerable advantages of preventive industrial medicine and surgery.

2. The full time industrial physician serving in one or several plants who exemplifies specialty practice in industrial health. In addition to prevention and treatment of compensable disability, he is concerned with the details of medical department administration.

3. The medical industrial hygienist more frequently associated with governmental agencies, who provides a consultative and investigative service directly to industry and to the medical profession, as well as enforcement of public health and sanitary codes relating to conditions of work.

In each of these classifications there are definite shortages of well trained personnel.[2] To meet these varying educational requirements, medical and professional schools and medical societies singly and in combination are under heavy obligation to create or improve opportunities for training in undergraduate and continuation courses and for extended graduate study.

CONTENT AND ORGANIZATION OF TEACHING

Experienced physicians in industry have testified that industrial health activity falls into three principal categories:

1. Industrial medical administration.
2. Industrial medicine and traumatic surgery.
3. Industrial hygiene and toxicology.

For physicians who expect to meet the ordinary medical needs of industry, proper grounding in each of these major subdivisions should be provided, begin-

1. Industrial Medical Education, J. A. M. A. **114**: 583 (Feb. 17) 1940.

2. Annual Congress on Industrial Health—Availability of Trained Industrial Health Personnel, J. A. M. A. **116**: 1455 (March 29) 1941.

ning in the undergraduate curriculum. The outline which is appended to this report has been prepared in recognition of these basic requirements to a well rounded understanding of industrial health service.

Actually only a few medical schools have made this type of instruction available. Industrial hygiene is widely taught as a relatively minor function of preventive medicine and public health. Problems in industrial medicine and surgery are presented without any relation to prevention and control over exposures and only as examples happen to present themselves in clinics or wards. Industrial medical administration has been almost completely ignored. Yet the experience of a number of medical schools amply demonstrates that reasonable acquaintance with the whole subject can be provided at modest expense through judicious use of time and readily available teaching and clinical material. The all important requirement for improved instruction is a unified plan which assigns over-all responsibility for coordinated classroom discussion, field studies, and laboratory and section work to one single teaching division, preferably preventive medicine and public health. There must always be considerable dependence on clinical teaching in the medical and surgical aspects of industrial practice, but the testimony of recent graduates clearly indicates that older methods of divided and unrelated instruction fail to provide dependable and reasonably complete information.

As a matter of fact, progress would be greatly accelerated if many more medical and graduate schools, especially those in industrial areas, could develop or attract support for the organization of separate teaching divisions in industrial health, each with its own faculty, affiliations for clinical and demonstration material and facilities for laboratory and field investigation and consultation. Good precedent exists for independent organization of this character. Under such an arrangement there should be greatly improved prospects for the attraction of special teaching talent and material, of support for research into a thousand aspects of industrial health crying for investigation and for the promotion of advanced training at graduate and fellowship levels.

PLAN OF INSTRUCTION

The essential requirements for teaching industrial health can most briefly be described as follows:

A. *Undergraduate Teaching.*

1. Required Courses: These courses should provide lectures, laboratory experience, industrial history taking and record keeping, section work in wards and clinics, and field trips in accordance with the accompanying outline.
2. Elective Courses: Electives should provide opportunity for more detailed and specific study, personal participation in special projects, individual patient study or personal experience in plant or laboratory. Time allotment will vary according to nature and extent of subject matter.

B. *Continuation Study.*

Since most practicing physicians have had little opportunity for organized instruction, introductory and refresher courses must be provided by universities, county, state and special medical societies or combinations thereof. The accompanying outline can serve as a model suitably modified to fit special requirements.

C. *Extended Study.*

The detailed course outline can serve as a framework for study, graduate in character, calculated to prepare physicians for full time specialty practice in industrial plants or industrial hygiene laboratories. Modifications will be necessary at such time as certification for industrial practice develops. More weight must be assigned to administrative details, personnel relations, legal and social medicine, toxicology, pathology, physiology and public health methods. Courses should be designed to establish competence in industrial health in its own right and not as a minor component of advanced teaching in public health.

OUTLINE OF A COURSE IN INDUSTRIAL HEALTH

The outline of a course in industrial health which follows is based on the three major constituents of medical service to employed groups—industrial hygiene, industrial practice and administration. Under each principal heading is incorporated a general statement explaining in broad terms its importance in the teaching program, followed by a more detailed listing of subheadings. Specific recommendations are also presented about teaching methods and facilities.

In general, the recommendations refer to required instruction for undergraduates. For more detailed instruction, suitable additions can readily be made or examples of existing syllabuses may be examined on application.

I. INDUSTRIAL HEALTH ADMINISTRATION

A. *General Statement.*

Present interest in working conditions and the welfare of workers follows a century of social and labor legislation which has culminated in workmen's compensation and social security enactments. As demands for industrial health supervision increase, physicians will be invited to organize and administer medical departments in factories, mines and stores of all types and sizes. The experience of many physicians in industry demonstrates that service of this nature can operate efficiently, ethically and scientifically and in full recognition of the best interests of worker, employer, official agencies, the general medical profession and the community at large.

B. *Organization for Teaching.*

With rare exceptions, well conducted industrial medical departments are readily accessible to most teaching centers. Directors of such departments are usually qualified to teach administrative procedure and to demonstrate it directly in the working environment.

About a third of assigned hours should be allotted to administrative methods equally divided between class room discussion and visits to acceptable plant medical departments.

C. *Course Content.*

1. Origin and Later Development of Industrial Health.
   (*a*) Clinical Interest in Occupation and Health.
   (*b*) Legislative Background.
      (1) Factory Acts.
      (2) Workmen's Compensation.
      (3) Social Security.
2. Occupational Morbidity and Mortality.
   (*a*) Causes and Duration of Lost Time in Industry.
      (1) General Experience.
      (2) Experience in Specific Industries.
   (*b*) Reportability of Industrial Accidents and Diseases.
3. Distribution of Industrial Health Service.
   (*a*) Scope and Objectives of Industrial Health.
   (*b*) Population Groups Involved:
      (1) According to Plant Size.
      (2) According to Type of Industry.
   (*c*) Costs of Medical Service in Industry.
   (*d*) Economic and Other Benefits.
4. Classification of Industrial Physicians.
   (*a*) On call and part time (detached).
   (*b*) Full time (attached).
   (*c*) Consulting services.
      (1) Industrial Hygiene.
      (2) Clinical Specialties.
   (*d*) Qualifications for industrial medical service.

5. The Industrial Medical Department.
   (*a*) Organization.
      (1) Personnel.
      (2) Plant and Professional Relations.
   (*b*) Quarters and Equipment.
   (*c*) Specific Functions.
      (1) Treatment and Hospitalization.
      (2) Prevention and Sanitation.
      (3) Health Conservation.
         (*a*) Physical Examinations.
         (*b*) Health Education.
      (4) Rehabilitation.
   (*d*) Special Medical Problems of Small Plants.

II. Industrial Hygiene and Toxicology

A. *General Statement.*

Employers and workers alike look to prevention as the cardinal principle for reducing the incidence of disability in industry. They have learned by experience that health conservation promotes efficiency, earning power and industrial relations. Physicians who serve in industry must be acquainted with dependable means for recognizing and controlling unhealthful occupational risk. The extraordinary development of industrial technology has multiplied these dangerous exposures tremendously. In addition to the procedures related to industrial hygiene and toxicology directly, there are equally important problems associated with adapting industrial medical activity to programs of adult hygiene in official and community health and welfare agencies.

B. *Organization of Instruction.*

Facilities and personnel necessary for adequate instruction in industrial hygiene are available singly or in combination through access to—

1. Bureaus of industrial hygiene in state or local governments.
2. Departments of biochemistry, physiology, clinical pathology and toxicology in the medical schools.
3. Suitably equipped independent or plant industrial hygiene laboratories.

About one third to one half of available hours should be allotted to industrial hygiene, toxicology giving equal consideration to didactic work and laboratory demonstration.

C. *Course Content.*

1. Industrial Health Exposures.
   (*a*) Classification.
   (*b*) Essential Toxicology.
   (*c*) Safe Concentration Codes.
2. The Plant Survey.
   (*a*) Identification of Exposures.
      (1) Medical Procedure.
      (2) Engineering Procedure.
   (*b*) Control of Exposures.
      (1) Medical.
      (2) Engineering.
   (*c*) Maintenance of Control.
   (*d*) Records.
3. Plant Sanitation and Hygiene.
   (*a*) Water Supply.
   (*b*) Waste Disposal.
   (*c*) General Housekeeping.
   (*d*) Illumination.
   (*e*) Ventilation and Air Conditioning.
   (*f*) Noise and Vibration Control.
4. Personal Hygiene for Workers.
   (*a*) Toilets and Washrooms.
   (*b*) Fatigue Control.
   (*c*) Nutrition.
   (*d*) Housing.
   (*e*) Recreation.
5. Coordination of Industrial and Community Health Service.
   (*a*) Communicable Disease Control.
   (*b*) Industrial Waste Control.
   (*c*) Vital Statistics.
   (*d*) Safety Codes and Regulations.
   (*e*) Factory Inspection and Regulation.

III. Industrial Medicine and Traumatic Surgery

A. *General Statement.*

Most medical service supplied to or through industry is aimed primarily at the individual worker suffering from compensable disability. Full restoration of the injured worker to his former earning capacity in the same line of work and without unnecessary delay is the ideal objective. The physician in industry must also recognize the considerable preponderance of nonoccupational injuries and disease as a factor in industrial absenteeism and the consequent necessity for proper correlation between industrial and private medical practice. This component of the training should also provide reasonable acquaintance with the industrial application of such commonly employed consulting services as dermatology, ophthalmology, neuropsychiatry, orthopedics, radiology and jurisprudence.

B. *Organization of Teaching.*

Clinical material in industrial medicine and surgery is abundant in most localities. Special affiliations and arrangements with agencies listed will be necessary:

1. Departments of surgery, medicine and jurisprudence in the medical school and with the principal related surgical and medical specialties (ophthalmology, dermatology, occupational therapy and so on).
2. Industrial outpatient clinics and hospital wards.
3. Industrial medical departments and dressing stations.
4. Workmen's compensation and rehabilitation agencies.

From one third to one half of available time should be assigned to industrial medicine and surgery. Principal emphasis should be placed on individual case study of ambulatory and bed patients with suitable supervision and correlated classroom discussion.

C. *Course Content.*

1. The Worker and the Job.
   (*a*) The Worker:
      (1) Physical and mental fitness.
      (2) Aptitude tests.
      (3) Medicine and personnel relations.
   (*b*) The Job:
      (1) Physical and mental requirements.
      (2) Duration—hours and wages, day, night, peak loads.
      (3) Special processes, equipment and working conditions.
      (4) Environmental factors.
2. Industrial Accidents.
   (*a*) Incidence and costs.
   (*b*) Classified causes.
   (*c*) Emergency care and transportation.
   (*d*) Surgical management.
   (*e*) Prevention.
   (*f*) Estimation of disability.
   (*g*) Records.
3. Occupational Diseases.
   (*a*) Etiologic classification.
   (*b*) Pathology and toxicology.
   (*c*) Medical Management.
   (*d*) Prevention.
   (*e*) Disability evaluation.
   (*f*) Records.
4. Nonoccupational Disability.
   (*a*) Incidence and costs.
   (*b*) Classified causes.
   (*c*) Medical advisory service.
   (*d*) Follow-up service.
   (*e*) Records.
5. Workmen's Compensation and Rehabilitation.
   (*a*) Administrative methods.
   (*b*) Medical relations and regulation.
   (*c*) Insurance practice.

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SATURDAY, FEBRUARY 28, 1942

GERMICIDAL GAS

The use of germicidal vapors for the prevention of air borne infection with influenza has been the subject of recent study by Robertson and his colleagues [1] of the Douglas Smith Foundation, University of Chicago. Demonstration that ferrets are readily infected by air borne influenza virus [2] has emphasized the possible clinical importance of physical or chemical methods of sterilizing the air. Successful sterilization by the use of ultraviolet radiation has been reported,[3] as well as the possibility of killing air borne bacteria and fungi by means of chemical mists (aerosols).[4] Robertson and his co-workers [5] found that glycol mists are effective, propylene glycol being the aerosol of choice because of its low toxicity.

Henle and Zellat [6] of the University of Pennsylvania afterward tested the same mists on influenza virus. Air streams from two atomizers were mixed in a 5 liter bottle. One atomizer contained diluted virus, the other either propylene glycol or water as a control. The concentration of glycol in the 5 liter mixture was approximately 1:200,000, as determined by loss of weight in the second atomizer flask. The virus-glycol mixture was then transferred to an exposure chamber containing 5 white mice. After forty-five minutes' exposure the mice were removed to individual cages. The death rate and the degree of pulmonary involvement of the survivors were determined on the eleventh day.

In control tests with water in the second atomizer, all mice exposed to undiluted virus in the first atomizer died between the sixth and the eleventh day. Half of the mice exposed to a 1:10 dilution of the same virus died before the eleventh day. In all survivors there were evidences of advanced pulmonary lesions. With a 1:100 dilution of the virus none of the mice died, though all showed some pulmonary involvement. With 1:1,000 dilution none died and but half of them developed pulmonary lesions. A 1:10,000 virus dilution was wholly noninfectious. Compared with this control series, a 90 to 99 per cent reduction in air borne virus infectivity was evident as a result of the presence of the 1:200,000 propylene glycol mist.

Robertson and his co-workers [7] found that the same glycol is ten times more effective against air suspended bacteria if used in the gaseous form. He afterward found that a 1:2,000,000 dilution of propylene glycol vapor would completely protect mice against dilutions of influenza A virus which regularly kill all control mice within four to ten days. These experiments indicate that 1:2,000,000 propylene glycol gas is an almost perfect germicidal agent when tested against air borne bacteria or air borne influenza virus. A direct clinical application of this experimental evidence, however, has not thus far been suggested by the Chicago investigators.

1. Robertson, O. H.; Loosli, C. G.; Puck, T. T.; Bigg, Edward, and Miller, B. F.: Science **94**: 612 (Dec. 26) 1941.
2. Andrewes, C. H., and Glover, R. E.: Brit. J. Exper. Path. **22**: 91 (April) 1941.
3. Wells, W. F., and Henle, W.: Proc. Soc. Exper. Biol. & Med. **48**: 298 (Oct.) 1941.
4. Twort, C. C.; Baker, A. H.; Finn, S. R., and Powell, E. O.: J. Hyg. **40**: 253 (May) 1940. Andrewes, C. H.: Lancet **2**: 770 (Dec. 21) 1940.
5. Robertson, O. H.; Bigg, Edward; Miller, B. F., and Baker, Zelma: Science **93**: 213 (Feb. 28) 1941.
6. Henle, W., and Zellat, J.: Proc. Soc. Exper. Biol. & Med. **48**: 544 (Nov.) 1941.
7. Robertson, O. H.; Bigg, Edward; Miller, B. F.; Baker, Zelma, and Puck, T. T.: Tr. A. Am. Physicians **56**: 353, 1941.

THE "ESSENCE" OF SULFONAMIDE QUACKERY

Physicians have recently been circularized by the Koch Laboratories, Inc., of 8181 East Jefferson Avenue, Detroit, with regard to an item which is called "1:4 Benzoquinone" or "BQ" and described as one of "Koch's Synthetic Antitoxins." The so-called 1:4 Benzoquinone is designated as the "active principle of the sulfonamide series." In the promotional material for 1:4 Benzoquinone appears a statement that it has been in use since 1922. The Journal has commented frequently [1] on the promotion of Koch's "Glyoxylide," which he claims was introduced at the same time. Since reference to the promotional material for Glyoxylide does not indicate any active promotion for Benzoquinone, this would seem to be essentially, if not technically, a new drug. The promotional material for 1:4 Benzoquinone (Koch) does not contain any references to medical writings to substantiate the claim that this is the active principle of the sulfonamide series. Neither is there any clinical evidence to support the statement "We recommend 1:4 Benzoquinone in the treatment of all infections, including . . . streptococcus sore throat, pneumonia, undulant fever" and "infantile paralysis" and several other conditions, including "the allergies." In view of prevailing federal drug legislation how can such promotional material as this be used? It is not unusual, however, for the Koch Labora-

1. The "Glyoxylide" of William F. Koch, J. A. M. A. **107**: 519 (Aug. 15) 1936. Koch Cancer "Cure" and the Canadian Cancer Commission, ibid. **116**: 2525 (May 31) 1941. Canadian Cancer Commission Denies Authorization for Circular on Koch Treatment for Cancer, Correspondence, ibid. **117**: 216 (July 19) 1941.

tories to promote preparations for treatment without the slightest real proof of their usefulness. The recommendation of the drug for such a wide variety of conditions is followed by a paragraph headed "Scientific Basis":

"Accurate catalytic dilutions of 1:4 Benzoquinone activate Oxygen in the tissues, spontaneously forming peroxides that split into Glyoxylide and Malonide, the most efficient catalysts of tissue oxidation that can exist.

"They burn the toxic groups in every pathogenic germ product, making them harmless to the body, and nonsupportive to germ life.

"They restore the tissue oxidations providing the energy for normal dispersion of the tissue colloids, for normal function and growth.

"1:4 Benzoquinone, Glyoxylide and Malonide have proven absolutely harmless since their first use in 1922. They were among our first Synthetic Antitoxins."

If that is scientific basis, it is apparently more confusing than scientific. Next follows a section headed:

"1:4 Benzoquinone (the Active Principle of the Sulfonamide Series). The members of the sulfonamide series may kill or cure. It depends upon whether or not the patient's oxidations are still active enough to burn off the amino group, the sulfonic acid group, and the other characterizing group, and oxidize the benzene ring to 1:4 Benzoquinone."

This astounding statement is wholly unsupported by evidence. The Koch Laboratories then suggests that, even though this Benzoquinone is formed, the balance of the sulfonamide preparation which has not been so converted serves to handicap the action of the Benzoquinone, whereas 1:4 Benzoquinone, in its proper dilutions, "works curatively only." Extravagance in statement proceeds to expansive exaggeration.

"This therapy with Glyoxylide and Malonide [are they the same as 1:4 Benzoquinone?—ED.] are the most scientific known. Their serviceability is UNIVERSAL and HARMLESS. There are no contraindications. One dose is generally sufficient."

The promotion next discusses "Case Management," which includes a dietary regimen and "good colon hygiene." "The recovery process," it proceeds, "is cyclical with a periodicity of three hours and its multiples, three and a half days and its multiples, and three weeks and its multiples." Is this astrology?

Under the heading of "Economy" one finds the statement "No method of caring for serious sickness compares in economy with this treatment." At $10 per 2 cc. ampule?

Entirely absent from this promotional material is any reference whatever to the use of the product in human beings or in animals. Nowhere is there any proof that the product has ever been used successfully in any of the conditions for which it is recommended. The statements about this item addressed to the medical profession smack of typical "patent medicine" promotion to the general public. Surely physicians today are sufficiently well educated to disregard such lucubrations.

THE ACCELERATED MEDICAL CURRICULUM

Elsewhere in this issue appears a resolution adopted by the Council on Medical Education and Hospitals of the American Medical Association, which presents its views concerning the acceleration of our medical curriculum in approved medical schools during the war period. The Council emphasizes the importance that each medical school determine for itself whether or not it can initiate such an accelerated curriculum and indicates the factors which may be considered in making the decision. As was stated in a previous editorial in THE JOURNAL on this subject, little would be gained by accelerating the medical curriculum if the results included a deterioration of the quality of medical education. Fortunately the Council on Medical Education and Hospitals is prepared to make necessary inspections in order to aid in maintaining our present high standards.

Coincidental with the meeting of the Council on Medical Education and Hospitals and the annual conference, meetings were held of the Association of American Medical Colleges and of the Federation of State Medical Boards. Both organizations also considered the proposals related to acceleration of the curriculum. A special report prepared by the Bureau of Legal Medicine and Legislation of the American Medical Association indicates that some states will have to revise their laws and others the regulations governing licensure for medical practice before it will be possible for students to obtain licenses to practice in such states. The Federation of State Medical Boards proposes to take the necessary steps to meet this difficulty although, obviously, there can be no assurance of the attitudes to be taken by state legislatures or of the time required to bring about necessary changes.

The Association of American Medical Colleges was also concerned with the fact that needy medical students may need help in completing the curriculum when time is not available in a vacation period for the earning of money. Apparently the federal government proposes to lend money to medical students along with students in other branches of learning so that they may complete the curriculum. The circumstances under which money will be lent are still subject to much consideration.

The actions taken emphasize some of the factors involved in acceleration of medical curriculum which were discussed in THE JOURNAL in its editorial "Speeding Production of Physicians," published on January 17. No doubt the months of experimentation to come will indicate many details of organization and of teaching and other considerations which will need to be integrated and coordinated with this proposal before it can function smoothly and efficiently. Obviously not all of the medical schools in the United States are going to be able to undertake the accelerated program with equal efficiency, yet the offer of federal funds paid either directly to the student or to the college may stimulate

many to undertake the project nevertheless. Much of the necessary integration and coordination should have been worked out before the proposal was first urged on the colleges.

At a conference of the Association of American Medical Colleges with the Council on Medical Education and Hospitals and with the Board of Trustees of the American Medical Association, held in Chicago on February 18, a liaison committee was appointed which will aid largely no doubt in overcoming some of the difficulties. Equally important will be proper relationship with the Federation of State Medical Boards and with the Association of American Universities, which will also have an interest in this matter. Finally, the Health and Medical Committee in the Office of Defense Health and Welfare, which is charged with coordination of policies relating to medicine, should give the entire matter its consideration. The Offices of the Surgeon Generals of the Army, Navy and Public Health Service and the Office of the Procurement and Assignment Service for Physicians, Dentists and Veterinarians may be able to develop a fairly accurate approximation of the number of trained personnel to be secured. On such an estimate the colleges might be able to base their decisions as to the number of additional students to be educated, the duration of the speeding up process that will be required and the number of prospective medical students of high quality that can be secured.

Current Comment

EXTREME PREMATURITY AND PERSISTENT TUNICA VASCULOSA LENTIS

Occasionally persistence of tunica vasculosa lentis is observed in full term infants. It is usually limited to one eye and is believed to be due to lack of involution, the result of a purely local disturbance. The presence of a grayish white opaque membrane behind each crystalline lens is reported by Terry[1] in a prematurely born 6 months old twin infant. Since this original observation, four similar ones have been observed in the clinic of the Massachusetts Eye and Ear Infirmary. All the infants were premature, all weighed 3 pounds (1.3 Kg.) or less and none presented evidence of hereditary factors. Terry states that it has not been determined whether this abnormal tissue is a persistence of the entire vascular structure of the fetal vitreous or a fibroblastic overgrowth of the persistent tunica vasculosa lentis. He believes that prematurity could be an important factor not only in preventing normal involution due to closure of the hyaloid artery but also in producing an overgrowth of supporting tissue. The occurrence of the condition in a group of five premature infants suggests the existence of some hitherto unrecognized factor in extreme prematurity which favors the development of this condition.

1. Terry, T. L.: Extreme Prematurity and Fibroblastic Overgrowth of Persistent Vascular Sheath Behind Each Crystalline Lens, Am. J. Ophth. 25: 203 (Feb.) 1942.

THE JAPANESE AND ILLICIT OPIUM TRAFFIC

Paragraph 15 of a booklet of regulations for Japanese soldiers reads as follows:

> The use of narcotics is unworthy of a superior race like the Japanese. Only inferior races, races that are decadent, like the Chinese, Europeans and East Indians, are addicted to the use of narcotics. This is why they are destined to become our servants and eventually disappear.

The role played by the "superior" race in the enslavement of the other races through the use of narcotics is revealed in a statement by the Secretary of the Treasury, Mr. Morgenthau (release to the press, January 26). Commissioner of Narcotics Harry J. Anslinger reported to the secretary that he had abundant proof that Japan had defied international commitments by promoting the opium trade. The Japanese officials had three objectives in their traffic: to gain revenue, to corrupt Western nations and to weaken and enslave the peoples of lands already invaded or marked for invasion. Wherever the Japanese army goes, the drug traffic follows. This illicit commerce in "white" drugs is more than tolerated by the Japanese government. It constitutes an important part of its aggressive policy. The extent of this traffic and the conditions engendered by it are truly appalling. According to our narcotic chief, not less than 90 per cent of all the illicit "white" drugs of the world are of Japanese origin, manufactured in the Japanese concession of Tsientsin, in Dairen or in other cities of Manchuria, Jehol and occupied China, and this always by Japanese or under Japanese supervision. The report states that the Japanese concession in Tsientsin has become the heroin center of China proper and of the world, and it is from here that not only the Chinese race but all other countries of the world are being weakened and debauched. The Japanese consulate at Chengchow in Honan acts as a center for the distribution of drugs. The report further states that since the invasion of North China by the Japanese all legal control of the narcotic trade has ceased to exist. This is another form of chemical warfare against the Chinese people as deadly as war gases. Japanese authorities derive revenue from this traffic to cover part of the costs of their invasion of China. The entire situation was aptly summed up in the statement of Lieutenant Commander Fletcher, made in the House of Commons on Dec. 22, 1938: "Pestilence and war are historically associated with each other, but it has been left to the Japanese to find a way of making a pestilence pay for war." This presumably is the "order and peace" and the "benefits of friendly collaboration" that the Japanese military are bringing to the people of China. We are directly concerned in the matter because of an alarming amount of smuggling of the "white" drugs into the United States. The statement reveals that by one gang of traffickers alone enough heroin was smuggled into the United States to supply ten thousand addicts for one year. One shipment seized in Seattle from four Japanese totaled a million shots of morphine. To combat this illicit traffic, a law was enacted by the United States in 1935 imposing heavy fines on the master or owner of any vessel visiting our ports on which unmanifested heroin, morphine or cocaine is found.

MEDICINE AND THE WAR

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medicine and the war, and such other information and announcements as will be useful to the medical profession.

PAYMENT OF INCOME TAX BY PERSONS IN MILITARY SERVICE

Although section 513 of the Soldiers' and Sailors' Civil Relief Act of 1940 permits the deferment of the payment of federal income taxes by persons in military service, the moratorium is not automatic. The taxpayer must show that his ability to pay the tax is materially impaired by reason of such service. Proof of that impairment should be submitted at the time the tax return is filed, on a form procurable from the offices of the collectors of internal revenue.

In order that physicians in military service who desire to take advantage of the deferment privilege may know the type of information that must be supplied to justify the request for deferment of the payment of the tax, the form is reproduced below:

STATEMENT OF FINANCIAL CONDITION

(For benefits under Section 513, Soldiers' and Sailors' Civil Relief Act of 1940)

Name..... Amount of income
Present tax liability.....
address..... Occupation before entering
..... military service.....

1. My present military service began on....., 19... for a period which will end on....., 19....
2. Average monthly salary for the year before entering military service $.....
3. Average monthly income, other than salary, for same year $.....
4. Statement of assets and liabilities as of this.....day of....., 19...:

Assets	Fair Market Value	Liabilities	Amount
Cash	$.....	Accounts payable	$.....
Accounts receivable	.....	Notes payable	.....
Notes receivable	.....	Real estate mortgages	.....
Automobiles	.....	Chattel mortgages	.....
Stocks and bonds	.....	Accrued real estate taxes	.....
Real estate	.....	Judgments	.....
Other assets	.....	Other liabilities	.....
Total assets	$.....	Total liabilities	$.....

5. Amount per month of military pay, including cash allowances $.....
6. Average per month of all other income (including any amount from former employer) received since entering military service $.....

AFFIDAVIT

I, ..., being duly sworn, depose and say that the foregoing list of assets and liabilities and other information disclosed above are true and complete in every respect.

Subscribed and sworn to before me this.....day of....., 19...

.....
(Signature and title of officer administering oath)
(SEAL)

.....
(Signature of Applicant)

YELLOW FEVER IMMUNIZATION FOR ALL ARMY PERSONNEL

Immunization of all Army personnel against yellow fever was ordered on February 12 by the War Department.

Secretary of War Henry L. Stimson announced on Feb. 6, 1941 that the Surgeon General of the Army had been directed to vaccinate all soldiers stationed in the tropical regions of the Western Hemisphere, including Panama and Puerto Rico. Soldiers going to those regions, and any other military personnel who desired it, were also vaccinated. This was the first step toward compulsory vaccination against yellow fever by the Army. The present order is a preventive measure designed to make all soldiers available for service in areas where the disease is known to exist.

Immunization of the U. S. Army will be the first large scale vaccinations against the tropical disease ever attempted by a military force. Immunization is accomplished by the subcutaneous injection of 0.5 cc. of diluted yellow fever vaccine. Only one injection is required. Yellow fever vaccine used by the Army consists of a special strain attenuated virus developed through prolonged cultivation in tissue cultures. The material is placed in ampules and is then rapidly frozen, desiccated, sealed and kept in the frozen state until used.

Yellow fever vaccine now being used is prepared in the laboratories of the International Health Division of the Rockefeller Foundation, New York City. Protective vaccinations given soldiers will grant immunity against "jungle yellow fever," which in 1932 was discovered to have its reservoir in jungle wild life. All soldiers are also given routine protective vaccinations against smallpox, typhoid-paratyphoid fever and tetanus.

COOPERATION BETWEEN RED CROSS AND DEPARTMENT OF WELFARE OF NEW YORK CITY

Conferences have been held between representatives of the American National Red Cross and the Department of Welfare of New York City in order to examine the task of caring for people suffering from bombing or other enemy activity. It was agreed that the responsibilities of the Red Cross for the care of people made needy by nature and accident caused disasters during peace or war are not affected by this memorandum. With regard to war caused emergencies, unanimous agreement was reached that responsibility for the various activities that need to be undertaken can be defined and allocated as follows:

1. *Rest Centers.*—A first requirement is the establishment of an adequate number of rest centers for the immediate and temporary care of noninjured sufferers of bombing or other belligerent action. This means providing emergency feeding, clothing and overnight sleeping accommodations for those in need of them. The Red Cross will assume responsibility for establishing, equipping and operating these rest centers. The total number and location of the rest centers will be determined after consultation by the Red Cross with the mayor, the Civil Defense authorities and the appropriate city departments.

The Red Cross will assume responsibility for feeding in these rest centers, utilizing facilities in the centers and mobile canteens and other field equipment where needed. Feeding will also be provided for defense workers at the centers and in the field as this may be needed. In the event of emergency situations which may exhaust the Red Cross supplies, the Department of Welfare will provide food from its communal feeding centers by way of temporary supplementation. Clothing will

be provided in the rest centers for those in need of it from Red Cross stocks and, so far as possible, from WPA clothing made available by the Department of Welfare on the request of the Red Cross.

2. *Communal Feeding.*—The Department of Welfare will assume responsibility for communal feeding by enlarging the facilities which it now maintains for mass feeding, and through other centers as they may be needed. Feeding may also be provided through restaurants on orders issued by the Department of Welfare. This communal feeding will be provided for civilian sufferers of belligerent action at all times when necessary, including the period after they have been assisted in rest centers and before they have been rehoused and established, so as to meet their own living needs.

3. *Rehousing—Cash Grants.*—The Department of Welfare will assume responsibility for finding housing facilities for those whose dwellings have been destroyed. It is anticipated that, except in extreme emergencies, sufferers from belligerent action will remain in the Red Cross rest centers from a few hours to a maximum of forty-eight hours. The Red Cross will keep the Department of Welfare continuously informed of the persons receiving care in rest centers, and the Department of Welfare will promptly assume responsibility for finding new dwellings. In all cases the Red Cross will continue to give assistance to affected families until the Department of Welfare assumes that responsibility. The Department of Welfare will also provide cash grants, as needed, and clothing. The Red Cross may provide supplemental assistance to that offered by the department, and the department will refer families and individuals to the Red Cross for that purpose. The Red Cross may undertake the repair of homes of those who have suffered from bombing, although major repairs and the rebuilding of homes will probably have to be deferred until after the termination of the war or of the emergency.

4. *Registration.*—The Red Cross will assume responsibility for providing information concerning civilians who have suffered from bombing or other belligerent action, so that prompt information concerning them can be given in reply to inquiries. The Department of Welfare and other public and private agencies giving any form of care or assistance will furnish a proper registration of such persons to the Social Service Exchange of the Welfare Council. The Red Cross will undertake to secure information through the Social Service Exchange in response to inquiries.

5. *Information.*—Subject to and in line with over-all plans for the giving of information in the city concerning welfare and social service open to the entire population, the Department of Welfare will be prepared to give information through its central office and its various branch offices throughout the city.

6. In accordance with plans already made, rescue, first aid and emergency medical care are responsibilities of the emergency medical service of the Defense Council. The Red Cross will assist, as requested, by providing emergency ambulances and other facilities, and by providing an adequate number of persons trained in first aid, as well as by training of nurses' aids.

7. As requested by the mayor, the Department of Welfare will undertake to coordinate the work of the private and social welfare agencies along the lines set up in this memorandum.

NORTHWESTERN HOSPITAL UNIT LEAVES FOR ACTIVE SERVICE

Fifty-eight physicians of U. S. Army Base Hospital Unit No. 12, the Northwestern Medical School Unit, left Chicago on February 15 for a short period of training at Camp Custer, Mich., and then for active military service at an unknown destination. One hundred and twenty-five nurses, the attendants and the remainder of the hospital staff had gone to Camp Custer previously. The head of the surgical staff of this unit is Dr. Michael L. Mason and the head of the medical staff is Dr. M. H. Barker. The members of the faculty of Northwestern University Medical School and the students entertained members of the hospital unit before their departure at a dinner at which the medical school chorus and the medical school orchestra performed.

LOCAL HEALTH DEPARTMENTS AND ILLINOIS DEFENSE ZONES

Governor Green has signed a new emergency law passed by the special session of the Illinois legislature which empowers the state department of public health to establish and maintain local health departments in areas which the department may define as defense zones. The new law amends that section of the Civil Administrative Code which prescribes the powers and duties of the state department of public health. At the request of any city or incorporated community situated in affected territories, the special wartime state health services may be extended to these municipalities as an aid to their existing local health agencies. According to the state department of public health there are now seven active military and naval establishments in Illinois which may be considered as defense zone centers: Fort Sheridan, Camp Grant, Great Lakes Naval Training Station, Chanute Field, Scott Field, Glenview Naval Air Field and Park's Air College.

AMERICAN COLLEGE OF SURGEONS HOLDS ONE DAY SESSIONS ON MILITARY MEDICINE

A series of special programs on medicine and surgery in military service and in civilian defense will be offered throughout the country to permit participation of medical and hospital professions in every state and the District of Columbia, under a cooperative plan of the U. S. Army, U. S. Navy and the Office of Civilian Defense with the American College of Surgeons. About thirty of these meetings will be held. A similar arrangement is contemplated in Canada. In the United States, meetings are planned in five areas. The first group is as follows:

AREA 1

Monday, March 2: Indiana and Kentucky, Brown Hotel, Louisville.
Wednesday, March 4: Arkansas and Tennessee, Andrew Jackson Hotel, Nashville.
Friday, March 6: Missouri, Jefferson Hotel, St. Louis.
Monday, March 9: Illinois, Stevens Hotel, Chicago.
Wednesday, March 11: Michigan, Statler Hotel, Detroit.
Friday, March 13: Ohio and West Virginia, Deshler-Wallick Hotel, Columbus.

The army will be represented at the meetings in Louisville, Nashville and St. Louis by Brig. Gen. Charles C. Hillman, Chief of Professional Service, Division, Office of the Surgeon General, and in Chicago, Detroit and Columbus by Major Roger G. Prentiss Jr., Medical Corps, Carlisle, Pa. The navy will be represented by Capt. Frederick R. Hook, Chief, Surgical Service of the U. S. Naval Hospital, Washington, D. C. The Office of Civilian Defense will be represented by Dr. William S. Keller, Glendale, Ohio, at the Louisville and Columbus meetings; by Dr. Judson D. Dowling, Birmingham, Ala., in Nashville, and by Dr. John S. Coulter, Chicago, in St. Louis, Chicago and Detroit. The Procurement and Assignment Service will be represented by Major Sam F. Seeley, Washington, Executive Officer, or by a specially appointed delegate.

Other speakers who will take part in the program in the first area are Drs. Irvin Abell, Rettig A. Griswold and Joseph E. Hamilton of Louisville; George W. Crile of Cleveland; George M. Curtis of Columbus; Evarts A. Graham, Vilray P. Blair and James B. Brown of St. Louis; Carl E. Badgley, Frederick A. Coller and Max M. Peet of Ann Arbor; Grover C. Penberthy of Detroit; Willis D. Gatch of Indianapolis; Edward William Alton Ochsner, Ambrose H. Storck and Michael E. DeBakey of New Orleans; Frederic A. Besley of Waukegan; Warren H. Cole, William R. Cubbins, Loyal Davis, Sumner L. S. Koch and Dallas B. Phemister of Chicago.

Among the subjects to be discussed in the program for the medical profession are treatment of war injuries to the skull and face; treatment of war injuries to the chest; the doctor and the hospital in civilian defense; treatment of wounds of soft parts; prevention and treatment of hemorrhage; treatment of burns and the prevention and treatment of shock. Every phase of hospital service, organization and maintenance will be treated in the program for hospital representatives.

PROMOTIONS IN THE NAVY

The President of the United States has approved the recommendations of the Medical Corps Selection Board which convened in the Navy Department in Washington, D. C., on January 5 and selected one hundred and thirteen naval officers of the rank of lieutenant for advancement to the rank of lieutenant commander and sixty-seven officers of the rank of lieutenant (j. g.) for advancement to the rank of lieutenant.

Following is a list of the officers recommended for promotion and their home addresses:

FOR LIEUTENANT COMMANDER

Douglas T. Prehn, Wausau, Wis.
James J. V. Cammisa, Boston.
Charles L. Ferguson, Waynesville, N. C.
Arthur W. Eaton Jr., Denver.
Cecil H. Coggins, Philadelphia.
William M. Silliphant, San Francisco.
Robert W. Babione, Luckey, Ohio.
Allan S. Chrisman, Charlotte N. C.
Calvin B. Galloway, Wyandotte, Mich.
Frank P. Kreuz Jr., Menominee, Mich.
James R. Reid Jr., Chester, S. C.
Austin J. Walter, Wheeling, W. Va.
Eugene V. Jobe, Eupora, Miss.
Albert H. Staderman, Philadelphia.
Paul M. Crossland, San Diego, Calif.
Alton C. Abernethy, Altus, Okla.
Earl F. Evans, New Orleans.
Walter H. Schwartz, Burlington, Iowa.
Armand J. Pereyra, San Francisco.
George N. Raines, Jackson, Miss.
William V. Clark, Lineville, Ala.
Edward T. Knowles, Oakland, Calif.
Lyle A. Newton, Hollinger, Neb.
James L. Holland, Meridian, Miss.
George F. Blodgett, Little Rock, Ark.
Judson A. Millspaugh, Jacksonville, Fla.
Albert W. Eyer, Washington, D. C.
John T. Smith, New Rochelle, N. Y.
Martin Van Brown, Carbondale, Ill.
Joseph V. Land, St. Louis.
Cecil L. Andrews, Greenfield, Ind.
Oran W. Chenault, England, Ark.
David C. Gaede, Loma Linda, Calif.
Robert A. Cooper, St. Paul.
Cecil D. Riggs, Philadelphia.
Jerry T. Miser, Alhambra, Calif.
Phillip S. McLennan, Decatur, Ga.
Edwin B. Coyl, San Diego, Calif.
Ralph K. Hoch, Woodside, Del.
Freeman C. Harris, Benton, Ill.
Thomas L. Allman, Milford, Ind.
Raphael L. Weir, Dickinson, N. D.
Edgar L. Nefflen, Elkins, W. Va.
Otto W. Wickstrom, Cambridge City, Ind.
Elmer L. Caveny, Atlanta, Ga.
Gordon H. Ekblad, St. Paul.
Ernest C. Aulls, Orlando, Fla.
Robert C. Boyden, Washington, D. C.
Robert C. Douthat, Kansas City, Kan.
Edward P. Madden, Salida, Colo.
Clifford F. Storey, Houston, Texas.
Julius C. Early Jr., Aulander, N. C.
Frederick R. Lang, Philadelphia.
Clark G. Grazier, Philadelphia.
John M. Wheelis Jr., San Diego, Calif.
William L. Engelman, Rockwell City, Iowa.
Robert L. Ware, Drexel Hill, Pa.
Robert A. Bell, Lone Tree, Iowa.
John J. Wells, Somerville, Mass.
Murphy K. Cureton, Rising Fawn, Ga.
Alvin J. Cerny, Chicago.
George B. Ribble, La Moure, N. D.
Paul K. Perkins, Chapell Hill, N. C.
Edward F. Kline, Lakewood Village, Calif.
Otto E. Van Der Aue, Chicago.
Howard K. Sessions, Sumner, Ga.
Langdon C. Newman, Covington, Ky.
Victor G. Colvin, Schellsburg, Pa.
Donald O. Wissinger, Logansport, Ind.
Adrain J. Delaney, Richmond Hill, N. Y.
Fitz-John Weddell Jr., Storkville, Miss.
Ralph D. Handen, Kingsville, Texas.
Leslie D. Ekvall, La Grange, Ill.
Ernest M. Wade, San Diego, Calif.
Joseph La Monte Zundell, Salt Lake City.
Giffin C. Daughtridge, Rocky Mount, N. C.
Benjamin G. Feen, Atlanta, Ga.
Harold J. Cokely, Rock Port, Maine.
Clarence F. Morrison, Sutton, W. Va.
James A. Price, Galveston, Texas.
Lawrence E. Bach, Washington, D. C.
John Henry Ward Jr., San Diego, Calif.
Ralph M. McComas, Peach Creek, W. Va.
Malcolm W. Arnold, Sardis, Miss.
Thomas L. Willmon, Cleborne, Texas.
James J. Sapero, Denver.
Francis K. Smith, Barrington, Ill.
James B. Butler, Swedesboro, N. J.
Andrew Galloway, John City, Ill.
George R. Hogshire Jr., Portland, Ore.
Marcy Shupp, Kansas City, Kan.
Frank Alexander Latham, Pontococ, Miss.
Eugene Rudolph Hering Jr., Shell Lake, Wis.
Erwin Herbert Osterloch, Nordheim, Texas.
Charles D. Bell, Minneapolis.
Paul Monroe Hoot, Ponca City, Okla.
Morris M. Rubin, Pasadena, Calif.
Louis M. Harris, Corpus Christie, Texas.
Charles R. Moon, Nashville, Ark.
Thomas W. McDaniel Jr., Boughton, Ark.
Stephen E. Flynn, Butte, Mont.
Harold E. Gillespie, Gradd Range, Mont.
Frank R. Urban, Riverside, Ill.
Edgar Ricen, Portland, Ore.
Paul Peterson, Wesson, Miss.
Alton Reginald Higgins, Lewiston, Maine.
Luther George Bell, Edgefield, S. C.
David H. Davis, Kansas City, Kan.
Lewis T. Dorgan, Great Bend, Kan.
Richard S. Silvis, Wagner, S. D.
Oscar Schneider, Hollywood, Calif.
Clifford P. Powell, Auburn, Ala.
Julian M. Jordan, Chicago.

FOR LIEUTENANT

Robert V. King, Lebanon, Mo.
George J. Kohut, Dickson City, Pa.
Ralph C. Parker, Jr., Batavia, N. Y.
William T. Foley, Flushing, N. Y.
Eldon C. Olson, McIntosh, S. D.
Robert E. Bruner, Powersville, Mo.
Boris Schuster, Stoughton, Wis.
Louis E. Daily, Baltimore.
Ralph B. Berry, Tyndall, S. D.
Joseph J. Zuska, Chicago.
Felix H. Ocko, Atlanta, Ga.
Jacque E. Miller, Shelby, Ohio.
Ronald B. Fankboner, Buhl, Minn.
Robert B. Jamieson Jr., Newton Center, Mass.
Karl J. Palmberg, Red Oak, Iowa.
Norman S. Hunt, Milwaukee.
Robert B. Johnson, York, Neb.
Howell E. Wiggins, Gablequah, Okla.
William S. Wray, Northfork, W. Va
Chalmers R. Carr, Mooresville, N. C.
Thomas M. Foley Jr., Washington, D. C.
George L. Calvy, Fond du Lac, Wis.
Francis W. Gross, Erie, Pa.
Joseph J. Blanch, Philadelphia.
George T. Ferguson, Kansas City, Mo.
Robert B. Greenman, New Lenox, Ill.
Joseph L. Yon, Charlottesville, Va.
Ralph W. Geise, Sunbury, Pa.
Roald N. Grant, Madison, Wis.
Edward L. Hammond, San Antonio, Texas.
Edward A. Anderson, Des Moines, Iowa.
Sylvester F. Williams, Wilmington, Ill.
William F. Queen, Louisa, Ky.
John W. Koett, Pittsburgh.
Derrick C. Turnipseed, Fitzpatrick, Ala.
Willam W. Ayres, New Orleans.
Bruno O. Junnila, Gheen, Minn.
Robert O. Canada Jr., Grottoes, Va.
Paul J. Ritchie, Los Angeles.
James A. Grindell, Mukwonago, Wis.
John D. Walters, Uniontown, Pa.
Marcellus C. Shurtleff, Strang, Neb.
Edward F. Szlosek, Nashua, N. H.
J. Francis Richardson, Cape Charles, Va.
Lamar B. Harper, Hyattsville, Md.
James E. Eppley, Princeton, Wis.
Arthur J. Vandergrind, Washington, D. C.
Peter P. Machung, Nanticoke, Pa.
Joseph M. Picciochi, Olyphant, Pa.
Norman L. Barr, Boyle, Miss.
Robert H. Mershon, Los Angeles.
Clement D. Burroughs, Little Rock, Ark.
Frederic G. Hirsch, Toledo, Ohio.
George W. Mast, Memphis, Tenn.
Emmett F. Norwood, Bremerton, Wash.
Vernon E. Martens, St. Louis.
Walter F. Berberich, San Pedro, Calif.
Shirley A. Fuhring, Washington, D. C.
Robert G. Gilbert, Rome, Ind.
Nicholas M. Musso, Washington, D. C.
Edward F. Ritter Jr., Mattoon, Ill.
John S. Shaver, Corsicana, Texas.
Leslie G. Seebach, Minneapolis.
John T. Cangelosi, Dunkirk, N. Y.
Wallace E. Allen, Modesto, Calif.
Lewis S. Sims Jr., Waynesboro, Ga.
Robert C. Ray, Garrison, N. D.

MEDICAL PREPAREDNESS IN CUBA

A committee on medical preparedness has been organized for the war, under the direction of Dr. Pedro L. Fariñas. This committee is integrated by delegates of the following medical organizations:

Academia de Ciencias Médicas, Fisicas y Naturales de la Habana
Sociedad de Estudios Clínicos de la Habana
Sociedad Nacional de Cirugia
Sociedad Cubana de Dermatologia y Sifilografia
Sociedad Cubana de Cardiologia
Sociedad Cubana de Oftalmologia
Sociedad Cubana de Tisiologia
Sociedad Cubana de Urologia
Sociedad Cubana de Pediatria
Sociedad de Gastroenterologia
Sociedad Cubana de Hematologia
Sociedad de Obstetricia y Ginecologia
Sociedad Cubana de Cancerologia
Sociedad de Microbiologia
Sociedad Cubana de Oto-Laringologia
Sociedad de Radiologia
Sociedad Cubana de Medicina Preventiva
Sociedad Cubana de Oropedia
Instituto Finlay
Sociedad de Enfermedades del Tórax
Sociedad Cubana de Salubridad Pública
Sonsejo Superior de Tuberculosis
Escuela de Medicina
Sanidad Municipal
Sociedad de Estudios Clínicos de Santiago de Cuba
Sociedad de Medicina y Cirugia de Santiago de Cuba
Sociedad de Estudios Clínicos de Camaguey
Sociedad de Medicina y Cirugia de Santa Clara
Sociedad de Medicina y Cirugia de Mantanzas
Sociedad de Estudios Clínicos de Cienfuegos
Colegio Estomatológico Nacional
Colegio Estomatológico de la Habana

Some other organizations closely related to the medical profession have been incorporated in the committee, including nurses, pharmacists and some others whose help has been considered valuable, as the Reporters' Association and women's social clubs. The work to be accomplished has been divided among six subcommittees, on Foods and Nutrition, Medical First Aid, Pharmacy, Preventive Medicine and Public Health, Technical Training and Medical Mobilization. A series of conferences was initiated. The first session took place at the Academy of Sciences on January 23 with a large attendance. A paper was read by Dr. Moises Chediak on "National Organization of the Services of Blood Transfusion" and one by Dr. Guillermo García López on "Importance of the Official Measures Aiming to Guarantee an Adequate Ration for the Population in All Possible Emergencies."

A complete overhauling of records has been undertaken. Questionnaires have been sent to the four thousand physicians who are members of the federation, and the results will be classified. Courses are organized for the technical training of young physicians, nurses and women, and attention is being given to those measures of preventive medicine, taking advantage of the national organization and coordinating with medical colleges in all municipalities of the island.

OPTICAL UNITS TO ACCOMPANY ARMIES IN THE FIELD

Mobile optical units which will accompany armies in the field have been organized, the War Department announced on February 11. Under a recently established policy, spectacles are supplied to soldiers without cost. This service will not be confined to bases behind the lines. Each optical unit will be compactly housed in a standard 2½ ton truck, which will be its base of operations as well as its means of transportation. A wide assortment of semifinished lenses will be stocked. These, as required, will be cut down to size, shaped, smoothed and beveled by equipment carried in the truck. Five men will operate each truck, which will carry twelve thousand pairs of lenses, eight thousand four hundred frames, six hundred pairs of extra temples and twelve hundred spectacle cases.

A single unit of this type will have a production capacity of sixty pairs, or one hundred and twenty single lenses, daily, which is estimated to be sufficient for the average requirements of an army of three hundred thousand men.

During the World War the Army maintained a base optical unit in Paris, which filled twenty-two thousand prescriptions for glasses in its four months of operation. Records disclose a close correlation in the percentage of military personnel requiring glasses then and now.

On the basis of experience tables of the principal optical suppliers of America, it is estimated that 99 per cent of spectacle requirements can be supplied by the assortment of lenses carried in the mobile units. Requirements of an extraordinary nature can be temporarily filled until supplied from the rear.

One of the mobile optical units has already been supplied, and negotiations are now under way to procure equipment for five more units.

NURSE SLAIN BY JAPANESE

According to the Presbyterian Hospital Bulletin of the City of Chicago, an Associated Press dispatch from Chungking, China, dated January 16 indicated that the Japanese had slain all American missionaries on Hainan, Chinese island, after the outbreak of war in the Pacific, including registered nurse Miss M. Burkwall, who graduated from the nursing school of the Presbyterian Hospital in 1931. Miss Burkwall's brother graduated from Rush Medical College in 1931 and since then has practiced in China.

R. O. T. C. SUMMER CAMPS TO BE DISCONTINUED AT CARLISLE BARRACKS

The commandant of the Medical Field Service School, Carlisle Barracks, announced on February 13 that the Reserve Officers' Training Corps summer camps at the Medical Field Service School at Carlisle Barracks, Pa., will not be held next summer. The summer camps, which have been conducted at the Carlisle Post every summer since 1921, included students from some of the most important medical schools in the country. Many other shortened courses have been instituted at the various army service schools, particularly the Medical Field Service School, for training of personnel.

ARMY RESERVE OFFICERS ORDERED TO ACTIVE DUTY

WAR DEPARTMENT

The following additional medical reserve officers have been ordered to extended active duty by the War Department, Washington, D. C.:

BINKLEY, Frank Carlton, 1st Lieut., Los Angeles.
BLUMBERG, Richard W., 1st Lieut., Nashville, Tenn.
BRACKEN, Frank L., 1st Lieut., Johnstown, Pa.
IMLER, Allison E., 1st Lieut., Philadelphia.
LYLE, John S., 1st Lieut., Concord, N. H.
NADEAU, Alexandre T., 1st Lieut., Pascagoula, Miss.
PALITZ, Laurence L., 1st Lieut., New York.
POLAN, Charles G., 1st Lieut., Minneapolis.
SELDEN, Joseph L., 1st Lieut., Faunsdale, Ala.
VAN VLACK, Hall Glesnor, Lieut. Colonel, Jamestown, N. Y.

THIRD CORPS AREA

The following additional medical reserve corps officers have been ordered to extended active duty by the Commanding General, Third Corps Area, which comprises the states of Pennsylvania, Virginia, District of Columbia and Maryland:

BASTACKY, Morris, 1st Lieut., Pittsburgh, Fort George G. Meade, Md.
BRINSFIELD, Irving Carlton, 1st Lieut., Vienna, Md., Carlisle Barracks, Pa.
CROOM, Arthur Bascom, 1st Lieut., Philadelphia, Carlisle Barracks, Pa.
DEGNAN, Philip Augustus, 1st Lieut., Washington, D. C., Fort George G. Meade, Md.
DOBBS, George, 1st Lieut., Washington, D. C., Fort Belvoir, Va.
DRAPER, William Bateman, 1st Lieut., Boonsboro, Washington County, Md., Fort Belvoir, Va.
FRANK, David, 1st Lieut., Philadelphia, Aberdeen Proving Ground, Md.
GELLER, Edward Irwin, 1st Lieut., Philadelphia, Fort Belvoir, Va.
HANSELL, Robert Joseph, Captain, Philadelphia, Camp Lee, Va.
HEIMBACH, James Alvin, Major, Altoona, Pa., Fort Belvoir, Va.
HENNING, Roger Ellsworth, 1st Lieut., Washington, D. C., Carlisle Barracks, Pa.
HOPKINS, Jesse Bruce, 1st Lieut., Bridgewater, Va., Camp Lee, Va.
JACOBS, Robert Samuel, 1st Lieut., Washington, D. C., Fort Eustis, Va.
JOHNSON, Walter Brenaman, 1st Lieut., Cumberland, Md., Fort George G. Meade, Md.
KATSUKI, David Ichio, 1st Lieut., Philadelphia, Aberdeen Proving Ground, Md.
KILLIUS, William Joseph, 1st Lieut., Johnstown, Pa., Camp Lee, Va.
KOENIG, Arthur Rudolph, Captain, Pittsburgh, Fort Story, Va.
KOUGH, Othello Springer, 1st Lieut., Uniontown, Pa., Aberdeen Proving Ground, Md.
KOSSOW, Maurice J., 1st Lieut., Washington, D. C., Fort Belvoir, Va.
LITCHBURN, David Thomas, Major, Washington, D. C., Fort George G. Meade, Md.
LOGAN, Thomas Megoawan, Captain, Philadelphia, Fort Eustis, Va.
McCENEY, Robert Sadler, 1st Lieut., Laurel, Md., Camp Lee, Va.
McNEILL, Willard Payne, 1st Lieut., Takoma Park, Md., Fort Belvoir, Va.
MAXWELL, James Dinsmore, 1st Lieut., Washington, Pa., Carlisle Barracks, Pa.
MELORO, Patrick Ralph, 1st Lieut., Philadelphia, Carlisle Barracks, Pa.
MILLER, Beveridge, Captain, Washington, D. C., Camp Lee, Va.
MINADEO, Anthony Ralph, 1st Lieut., Erie, Pa., Camp Lee, Va.
MONTGOMERY, Edward Samuel, 1st Lieut., Tarentum, Pa., Fort Monroe, Va.
OMBRES, Severn Richard, 1st Lieut., Meadville, Pa., Fort Myer, Va.
PRICE, Weldon Aubrey, 1st Lieut., Arlington, Va., Camp Lee, Va.
PUGH, James Edwin, 1st Lieut., Yeadon, Pa., Edgewood Arsenal, Md.
REILLY, Francis St. Clair, Major, Blairsville, Pa., Aberdeen Proving Ground, Md.
ROYE, Wyatt Earle, 1st Lieut., Covington, Va., Fort George G. Meade, Md.
SALASKY, Milton, 1st Lieut., Norfolk, Va., Fort Belvoir, Va.
SATTERTHWAITE, Richard Wampler, 1st Lieut., Baltimore, Carlisle Barracks, Pa.
SAUL, Theodore Joseph, 1st Lieut., Dushore, Pa., Edgewood Arsenal, Md.
SPALDING, Henry Cannon, Captain, Richmond, Va., Fort Myer, Va.
SPANUTH, John Roy, Captain, Reading, Pa., Aberdeen Proving Ground, Md.
SWIFT, Shelley Allender, 1st Lieut., Philadelphia, Carlisle Barracks, Pa.
WARREN, Charles Weston, 1st Lieut., Upperville, Va., Camp Lee, Va.
WHITE, Matthew James Walter, Jr., 1st Lieut., Luray, Va., Fort Belvoir, Va.

Orders Revoked

BATTAGLIA, Frederick I., 1st Lieut., McKeesport, Pa.
BENSY, Oliver Robert, Captain, Pittsburgh.
BRINDISI, Gaetano, 1st Lieut., Philadelphia.
DITCHBURN, David Thomas, Major, Washington, D. C.
HAZLETT, Frank D., Captain, Washington, Pa.
ROGERS, William H., 1st Lieut., Lansdowne, Pa.
SAGERSON, Robert P., 1st Lieut., Johnstown, Pa.

ORGANIZATION SECTION

MEDICAL LEGISLATION

DISTRICT OF COLUMBIA

Changes in Status.—S. 2154 has been reported to the Senate, proposing to amend the healing arts practice act of the District of Columbia by imposing a citizenship requirement on applicants for licenses to practice the healing art. H. R. 6483 has passed the House, proposing to authorize the appropriation of $50,000,000 to enable the Federal Works Administrator to provide in and near the District of Columbia such housing, public works and equipment therefor, including hospitals and other places for the care of the sick, as may be necessary to relieve shortages due to defense activities.

MEDICAL BILLS IN CONGRESS

Change in Status.—H. R. 6548 has passed the House and Senate, making appropriations to supply deficiencies in certain appropriations for the fiscal year ending June 30, 1942. This bill, among other things, appropriates an additional sum of $2,500,000 for use by the United States Public Health Service in venereal disease control work. Of this amount $2,250,000 will be allotted to the states. An additional sum of $600,000 is appropriated for use by the United States Public Health Service for the training of nurses, an additional sum in the amount of $1,295,000 for emergency health and sanitation activities and an additional amount of $77,481 for disease and sanitation investigations.

Bills Introduced.—S. 2246, introduced by Senator Maybank, South Carolina, proposes to extend the benefits of the Soldiers' and Sailors' Civil Relief Act of 1940 to all persons who are registered under the Selective Training and Service Act of 1940, as amended, and are classified thereunder after physical examination as being available and fit for general military service. S. 2261, introduced by Senator Doxey, Mississippi, proposes to extend the benefits of the Soldiers' and Sailors' Civil Relief Act of 1940 to any obligation incurred by a person on or after the date of the enactment of the act and prior to the commencement of his period of military service if (1) such obligation is secured by a mortgage, trust deed or other security in the nature of a mortgage on a dwelling house owned by such person at the commencement of this period of military service and still so owned by him; (2) such house is used by his family or other dependents as a home; and (3) such mortgage, deed or other security is insured under the National Housing Act, as amended. H. R. 6527, introduced by Representative Case, South Dakota, proposes that persons who have served in the armed forces of the United States since Dec. 6, 1941 and prior to the cessation of hostilities in the present war shall be entitled to receive the same domiciliary or hospital care, including medical treatment, as is provided by law or veterans' regulations for veterans of the World War in like cases.

STATE MEDICAL LEGISLATION

Kentucky

Bills Introduced.—H. 207 proposes to provide for state reimbursement to hospitals for services rendered to indigents injured in motor vehicle accidents. A hospital is defined as any institution registered and approved by the state board of health which receives and cares for patients suffering from motor vehicle injuries. H. 242 proposes to provide for the licensing, inspecting and regulating by the state board of health of all hospitals and clinics within the state. Hospital is defined as "any institution which maintains and operates organized facilities for the diagnosis, care or treatment of human illness or injury, including convalescence and care during pregnancy, where persons may be admitted for overnight stay or longer." Clinic is defined to mean "any place, except the private office of a person holding a valid certificate as a duly licensed practitioner of the healing art, in which are maintained and operated organized facilities for the diagnosis or treatment of human illness or injury, or conduct of physical, mental or obstetrical examinations, which serves only persons who remain in said place for less than overnight stay." H. 248, to amend the pharmacy practice act, proposes that nothing in the act shall prevent any person from compounding or manufacturing his own particular product if such person has had fifteen years' or more experience in the compounding or manufacturing of his own particular products under the immediate supervision of a registered pharmacist, or if such person compounds or manufactures his own product under the immediate supervision of a registered pharmacist, or under the supervision of a graduate chemist of recognized standing, after the formula for such product has been approved by the state board of health. H. 315 proposes to exempt from the operation of the uniform narcotic drug act the "administering, dispensing, or selling at retail of any medicinal preparation that contains in one fluid ounce or if a solid or semisolid preparation, in one avoirdupois ounce, not more than one grain of codeine or of any of its salts." The present law exempts from the operation of the act the prescribing, administering, dispensing or selling at retail of any medicinal preparation that contains in 1 fluidounce, or, if a solid or semisolid preparation, in 1 avoirdupois ounce, not more than 2 grains of opium, not more than ¼ grain of morphine or of any of its salts, not more than 1 grain of codeine or of any of its salts, not more than ⅛ grain of heroin or of any of its salts, and not more than one of any of said drugs.

Bill Enacted.—S. 35, to create city and county boards of health in counties containing a city of the first class, provides, among other things, for the maintenance of laboratories and clinics necessary for the public health and for the maintenance of a psychiatric clinic. The director of health must be a physician, qualified as a public health administrator and shall be duly qualified and licensed, or eligible for license, as a medical practitioner in Kentucky.

Michigan

Bills Introduced.—H. 15-XX, to amend the communicable disease control act, proposes that it shall be the duty of the state commissioner of health to manufacture, purchase and distribute to health officers and health boards of counties, cities, villages and townships within the state, on requisition, antitoxin, biologic products and other products for use in the control of communicable diseases. H. 16-XX proposes to provide for the compulsory detention and treatment of any person afflicted with venereal disease who has either failed or refused to comply with any order of the state commissioner of health or who is unable or unwilling to conduct himself and to live in such a manner as not to expose members of his family or household or other persons with whom he may be associated or come in contact to danger of infection. The bill proposes that the probate court of any county may enter an order directing that such person be admitted to an approved hospital or institution established for the care of persons suffering from venereal disease; but the individual may not have denied to him the right to select the physician or the mode of treatment of his choice. Where such individual is unable to pay, the cost of the treatment may be made a charge against the county from which the person is committed; otherwise the person may be made to pay all or such part of the expenses as he is able to bear. The bill further provides that any physician discovering a case of venereal disease shall report same within twenty-four hours on blanks furnished by the state commissioner of health.

Bills Passed.—The following bills passed the senate, February 17: S. 16-XX, proposing that the cost of hospital services and materials furnished in the care of afflicted children shall not exceed a maximum of $5 per day, and S. 17-XX, proposing that

the hospital rate for services, appliances and other necessities furnished to crippled children shall not exceed the sum of $5 per day.

New Jersey

Bill Introduced.—S. 70 proposes to enlarge the state board of health to thirteen from twelve members and proposes that at least one member of such board be an optometrist.

New York

Bills Introduced.—S. 627, to amend the workmen's compensation law, provides for the rendering of dental care to an injured employee by any dentist selected by the employee. S. 664, to amend the workmen's compensation act, would authorize the industrial board to make an award to a physician or a hospital for medical care in amounts claimed or decided by an arbitration committee. S. 680, to amend the education law, proposes that x-ray diagnosis be deemed the practice of medicine and defines x-ray diagnosis as "that method of medical practice in which demonstration and examination of the normal and abnormal structures, parts or functions of the human body are made by use of x-rays, and any person who holds himself out to diagnose or able to make or makes any interpretation or explanation by word of mouth, writing or otherwise of the meaning of a fluoroscopic or registered shadow or shadows of any part of the human body made by the use of x-rays, and also the use of x-rays or radium for the treatment of any human ailment." S. 697 proposes an appropriation for the state department of health for use in furthering and promoting a broad nutrition program throughout the state, including the combating of food fadism. S. 847, to amend the judiciary law and the civil practice act, proposes to authorize a judge to appoint one or more physicians to examine an injured person and to furnish a written report thereof. The bill also makes provision for the payment of a reasonable fee to such experts. S. 788 and A. 964, to amend the insurance law, would authorize the writing of insurance against an obligation of the insurer to pay medical, hospital, surgical and funeral benefits to injured persons, irrespective of legal liability of the insured. A. 747 would amend the uniform narcotic drug law by exempting therefrom administering, dispensing or selling at retail of Stokes expectorant or Browns mixture, or any medicinal preparations other than Stokes expectorant or Browns mixture that contains in 1 fluidounce, or, if a solid or semisolid preparation, in 1 avoirdupois ounce, not more than 1 grain of codeine or of any of its salts. A. 803, to amend the civil rights law, proposes that no person shall be deprived of any right to exercise a license to engage in any profession, trade, business or calling because of service in the armed forces of the United States during the period of the present war, or for six months after his discharge from such service. A. 895, to amend the unemployment insurance act, proposes that "if an employee become sick or incapacitated after he has begun to receive benefit payments, he shall continue to receive such payments upon presentation of a doctor's certificate showing such sickness or incapacitation, until such time as he is able to again report to the unemployment insurance office or has received his maximum allocation of payments."

South Carolina

Bill Introduced.—H. 1192, to amend the law relating to the issuance of marriage licenses, proposes as a condition precedent to the issuance of a license to marry that each party to a proposed marriage present a certificate signed by a licensed physician that the party is (1) free from venereal disease and tuberculosis in an infectious or communicable stage, (2) of sound mind, (3) not subject to epileptic fits and (4) not an idiot or an imbecile.

Virginia

Bills Introduced.—S. 178, to amend the insurance law, proposes to authorize corporations issuing motor vehicle liability insurance to add endorsements thereto for the issuance of medical, surgical, ambulance or hospital payments to the insured. S. 189, to amend the medical practice act, proposes to authorize the state board of medical examiners to admit to examination all applicants who have completed in not less than thirty-two months the four courses of at least eight months each required by the present law. Under the present law such four courses must have been given in four different calendar years. S. 125, to amend the workmen's compensation act, proposes to make compensable some twenty-five stated occupational diseases.

OFFICIAL NOTES

THE ATLANTIC CITY SESSION

Hotel Reservations

Fellows of the Scientific Assembly of the American Medical Association who expect to attend the annual session of the Association in Atlantic City, June 8-12, are urged to make their hotel reservations at the earliest possible time. For such reservations please send your first, second and third choice for a hotel reservation to Dr. V. Earl Johnson, Chairman of the Hotel Committee, 16 Central Pier, Atlantic City, N. J., in accordance with the information contained on advertising page 36 of this issue of THE JOURNAL.

WOMAN'S AUXILIARY

Pennsylvania

The Schuylkill auxiliary recently held the annual Health Institute in Pottsville. This was the sixth institute given by the Schuylkill auxiliary. Dr. Stanley P. Reimann, Philadelphia, pioneer in the field of cancer, was the principal speaker. Dr. Reimann also answered questions from the audience, after which a motion picture, "Choose to Live," was given. A film on tuberculosis was explained by Dr. Wilton R. Glenney, Pottsville, and a third picture on syphilis entitled "With These Weapons" was shown. The institute was opened by Mrs. Charles V. Hogan, president of the auxiliary. Mrs. J. William Jones was chairman of the institute, which was conducted in cooperation with the Women's Field Army.

The Lycoming auxiliary met recently in Williamsport. A letter from England citing the need for surgical instruments was read, and Mrs. J. Stanley Smith and Mrs. Carl H. Senn were appointed as a committee to attempt to procure these instruments. A letter of acknowledgment was read by Mrs. Senn, treasurer, for the sterilizer recently bought by the auxiliary for the Williamsport Hospital; also a letter of appreciation for $250 received for the Medical Benevolence Fund. Both gifts were made possible through proceeds received from the Medical Auxiliary Ball. Five dollars was donated for the local Salvation Army youth project.

The Lycoming County auxiliary's annual ball attracted more than 1,000 members and guests, and netted $1,300 to support the objectives of the auxiliary. Mrs. P. Harold Decker was chairman of the ticket committee. Of the $1,300 realized from the dance, $600 has been earmarked for the purchase of a sterilizer for the City Hospital and $250 more for the Medical Benevolence Fund of the state medical society.

Wisconsin

Mrs. S. A. Theisen was hostess to eighteen members of the Woman's Auxiliary to the Fond du Lac County Medical Society, recently. Mrs. D. F. Gosin of Green Bay, president of the state auxiliary, was a speaker. An appropriation was voted for the Children's Home. Mrs. Claude Musolf spoke on the Girl Scout troop sponsored by the auxiliary.

At the luncheon meeting of the Woman's Auxiliary to the Medical Society of Milwaukee County, recently, fifty-four members and sixteen guests, including Dr. Timothy Howard, president of the Milwaukee County Medical Society, were in attendance. Dr. James Sargent, past president of the Wisconsin Medical Society, spoke on the "Oath of Hippocrates." Mrs. William Liefert, chairman of Volunteers for Defense Committee, asked ex-registered nurses among the doctors' wives to help teach home nursing for the Red Cross.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ADDITIONAL MEDICAL COLLEGE NEWS AND ARTICLES APPEAR IN THE STUDENT SECTION, PAGE 757.

CALIFORNIA

Meeting of Study Club.—The Research Study Club of Los Angeles held its eleventh annual midwinter postgraduate clinical course in ophthalmology and otolaryngology, January 19-30. A feature this year was a special course on "Applied Anatomy and Cadaver Surgery of the Head and Neck," January 22-28, under the direction of Drs. Simon H. Jesberg, associate clinical professor of surgery, University of Southern California School of Medicine, Los Angeles, and Samuel A. Crooks, associate professor of anatomy, College of Medical Evangelists, Loma Linda. Guest speakers in the regular course on ophthalmology and otolaryngology were Drs. Ralph I. Lloyd, Brooklyn, and John R. Lindsay, Chicago.

Society News.—Dr. John H. Lawrence, San Francisco, addressed a joint meeting of the Los Angeles County Medical Association and the junior section of the Los Angeles Surgical Society, January 9, on "The Cyclotron and Its Application to the Practice of Medicine."——The Los Angeles Obstetrical and Gynecological Society was addressed, February 10, among others, by Drs. George W. Hewitt, Los Angeles, on "The Sudden Ruptured Pelvic Abscess" and George E. Judd, Los Angeles, "General Peritonitis—Recent Improvements in Treatment."——Dr. Kenneth S. Davis, Los Angeles, addressed the Los Angeles Surgical Society, February 13, on "Roentgenologic Diagnosis, Lesions of the Small Bowel."

Medical Committee to Study Industrial Problems.—The San Francisco County Medical Society has appointed a committee on industrial health which is prepared to study the individual health problems of industrial establishments in San Francisco without charge. The committee aims to cooperate with plant officials in devising means to reduce and remove needless health and accident hazards. Where special engineering procedures or prolonged medical studies are advisable, the committee will recommend competent persons to carry them out. The committee sent a letter and questionnaire to the managers of all firms in the city and county of San Francisco employing fifty or more persons in an effort to ascertain what specific problems may be their consideration. In the belief that many plants could establish industrial medical services which would pay substantial dividends in reduced compensation costs, increased efficiency and improved personnel relationship, the committee will help organize medical departments at the request of interested managements. All information exchanged between the committee and the plant is to be confidential. Members of the new committee are Drs. Rodney R. Beard, chairman, Nelson J. Howard and John Lawrence Brown, all of San Francisco.

CONNECTICUT

State Society to Supervise Merit System Examinations.—At the request of Mr. Harry W. Marsh, state personnel director, the Connecticut State Medical Society has accepted the responsibility for the organization and supervision of competitive examinations of physicians seeking public employment in the state merit system. Announcement has been made of examinations to fill appointments as crippled children physician, child hygiene physician, senior physician (psychiatric), assistant physician and supervisor of medical services (welfare).

Forum on Health in Industry.—At a recent meeting of the executive committees on industrial health of the Manufacturers' Association of Connecticut and the state medical society it was decided that future activities be devoted to preparing for a one day clinic or forum on health in industry and to developing standards for industrial medicine medical service, physical examinations and record forms. All groups interested in furthering industrial health in Connecticut will be invited to assist in arranging the program for the clinic, and steps will be taken to unify the aims of these various organizations.

DELAWARE

Special Military Program.—The New Castle County Medical Society presented a special military program for its members at the Academy of Medicine, Wilmington, February 17. The speakers included:

Lieut. Col. Arthur G. Compton, M. C., U. S. Army, Fort Du Pont, Problems Met by a Medical Officer on Duty in an Army Hospital.
Capt. Joseph R. Beck, M.C., U. S. Army, Fort Du Pont, Problems Met by a Medical Officer on Duty with Tactical Troops in the Field.
First Lieut. Robert M. Edelman, M. C., U. S. Army, Fort Du Pont, Demonstration of a Rapid Method of Blood Typing of Large Groups.
Dr. William H. Speer, Wilmington, The Function of the Office for the Procurement and Assignment of Physicians for the Army and Navy.

GEORGIA

Atlanta Clinical Society Lectureship.—Lectures will be delivered at the Academy of Medicine, Atlanta, March 5-6, under the auspices of the Atlanta Clinical Society. The speakers will be Dr. John B. Youmans, associate professor of medicine, Vanderbilt University School of Medicine, Nashville, Tenn., on "The Nutrition of Populations with Particular Reference to War Time Conditions," March 5, and Comdr. Charles S. Stephenson, U. S. Navy, Washington, D. C., "Medical Military Observations in England," March 6.

ILLINOIS

Personal.—Dr. Joseph A. Campbell has resigned as managing officer of the East Moline State Hospital.——Dr. Joe H. Price has resigned as state district health superintendent at McLeansboro. Until further notice Dr. Joseph L. Bryan, Xenia, of the Flora office will take over the work in Hamilton and White counties included in this district, and Dr. Roy W. Harrell of the Carbondale office will take over the work in Williamson, Saline, Gallatin and Franklin counties.

Psychiatric Research Council.—Dr. Harry R. Hoffman, state alienist, has been appointed chairman of the Illinois Psychiatric Research Council. Other members of the council which were announced by Governor Green on January 27 include the following, all of whom are of Chicago:

Dr. Peter Bassoe, professor of neurology, University of Illinois College of Medicine.
Dr. Lewis J. Pollock, professor of nervous and mental diseases, Northwestern University Medical School.
Dr. Francis J. Gerty, professor of psychiatry at Illinois.
Dr. John J. Madden, associate professor of neurology and psychiatry and chairman of the department, Loyola University School of Medicine.
Dr. David Slight, professor of psychiatry, University of Chicago, the School of Medicine.
Dr. Paul L. Schroeder, professor of psychiatry and criminology at Illinois.
Mr. John Nuveen Jr., chairman of the state board of welfare commissioners.

The purpose of the council is to facilitate the function and provide for the permanent maintenance of cooperative relations in teaching and research between universities and the department of public welfare of Illinois.

Chicago

The Bacon Lectures.—Dr. Jennings C. Litzenberg, professor emeritus of obstetrics and gynecology, University of Minnesota Medical School, Minneapolis, will deliver the Charles Sumner Bacon Lectures for 1941-1942 in the Medical and Dental College Laboratories Building of the University of Illinois College of Medicine, March 18-19. His subjects will be "The Significance of the Decreased Maternal Mortality Rates" and "Tradition and Truth Concerning Ectopic Pregnancies."

Elective Course in Endocrinology.—The University of Chicago has announced a special group of lectures in an elective course in endocrinology during the winter quarter. Among the instructors are Fred C. Koch, Ph.D., emeritus professor and chairman of the department of biochemistry; Carl R. Moore, Ph.D., professor and chairman of the department of zoology; George W. Bartelmez, Ph.D., professor of anatomy; Dr. Allan T. Kenyon, professor of medicine; Drs. Samuel Soskin, Franklin G. McLean, Arno B. Luckhardt, Victor Johnson and F. Joseph Mullin, Ph.D., and Howard Mauthe, Ph.D.

New Blood Donor Service.—A blood donor service center has been opened in the Blum Building, 624 South Michigan Avenue, under the auspices of the Chicago chapter of the American Red Cross. Blood donated will be processed into blood plasma at the Abbott Laboratories in North Chicago, to be available for emergency uses and by the armed forces. Dr. Sidney O. Levinson, director of the Samuel Deutsch Serum Center of Michael Reese Hospital, is the technical director. He will also be in charge of a medical advisory board, members of which include Drs. Herman Bundesen, health commissioner of Chicago; James P. Simonds, president of the Chicago Medical Society; Malcolm T. MacEachern, associate director

of the American College of Surgeons, and Joseph L. Baer of the Institute of Medicine of Chicago. The center will be open from 9 in the morning to 5 in the evening each day except Sunday. Donations from donors will be accepted by appointment only.

Memorial to Dr. Cutter.—The Council on Medical Education and Hospitals of the American Medical Association sponsored a meeting in the Assembly Hall of the Association headquarters on Monday evening February 16 to honor the memory of the late Dr. William Dick Cutter, Secretary of the Council since 1931. The meeting was held during the two day Annual Congress on Medical Education and Licensure at the Palmer House. The speakers were Dr. Ray Lyman Wilbur, Stanford University, Calif., whose address was entitled "Cutter, the Medical Administrator"; Dr. Charles Gordon Heyd, New York, "Cutter, the Medical Educator," and Alphonse M. Schwitalla, S.J., St. Louis, "Cutter, the Man." Dr. Wilbur, who presided, read the letters of tribute sent from all parts of the country. The three principal papers offered as part of the memorial were inspiring testimony to Dr. Cutter's reputation as an able administrator and marked his great contribution to medical education.

Interprofessional Meeting on War Activities.—More than twelve hundred physicians, dentists and veterinarians from northern Indiana, northern Illinois and southern Wisconsin met in the Museum of Science and Industry, Chicago, Sunday afternoon February 22 at a meeting sponsored by the Chicago Medical Society for the purpose of explaining the role the three professions will play in the nation's war effort. Speakers were Dr. Charles H. Phifer, chairman of the Procurement and Assignment Committee for the Sixth Corps Area; Major Sam F. Seeley, executive director, Procurement and Assignment Service, Washington, D. C.; Col. Paul G. Armstrong, director of selective service for Illinois, and Dr. Morris Fishbein, Editor of THE JOURNAL. Dr. James P. Simonds, president of the Chicago Medical Society, presided. Dr. H. Prather Saunders, chairman of the medical preparedness committee of the Chicago Medical Society, had charge of arrangements. Cooperating in holding the meeting were the Chicago Dental Society and the American Veterinary Medical Association.

LOUISIANA

Dr. Kostmayer Named Acting Dean at Tulane.—Dr. Hiram W. Kostmayer, professor of clinical gynecology and director of the department of graduate medicine, Tulane University of Louisiana School of Medicine, New Orleans, has been appointed acting dean of the medical school during the absence of Dr. Maxwell E. Lapham, who has been assigned to special duty in the Bureau of Medicine and Surgery, U. S. Navy. Dr. Lapham left for Washington on February 13.

Society News.—The Orleans Parish Medical Society devoted its meeting, January 26, to a symposium on tumors of the central nervous system. The speakers were Drs. Hugh Page Newbill, Herbert Randolph Unsworth, Lewis A. Golden, Gilbert C. Anderson and Dean H. Echols. All are from New Orleans. The society was addressed recently by Sidney W. Bliss, Ph.D., on "Enrichment of White Flour with Vitamins"; Drs. John H. Musser and Robert H. Onstott, "Venereal Disease Among Selectees and Volunteers in Louisiana," and Henry D. Ogden, "Modern Concepts in the Treatment of Bronchial Asthma."

Public Health Meeting.—The eighteenth annual meeting of the Tuberculosis and Public Health Association of Louisiana was held at the Washington-Youree Hotel, Shreveport, January 27-28. Dr. Julius L. Wilson, New Orleans, gave the presidential address on "The Place of Voluntary Tuberculosis Associations in Statewide Programs." Other speakers included:

Dr. Henry C. Sweany, Chicago, The Pathogenesis of Tuberculosis and Application of the Knowledge in the Control of the Disease.
Dr. William J. Sandidge, Shreveport, Case Finding Through the Health Unit.
Dr. Herbert N. Barnett, Benton, Cooperation of Health Units with Tuberculosis.
Dr. Russell H. Frost, Monroe, Procedures After the Tuberculous Patient Is Found.
Dr. Sydney Jacobs, New Orleans, Ambulatory Treatment of Tuberculosis.

NEW JERSEY

Society News.—Dr. William H. Perkins, Philadelphia, will address a meeting of the Fifth Councilor District of the Medical Society of New Jersey, March 13, at Northfield, on "Untapped Resources in Preventive Practice."——At a recent meeting of the Cumberland County Medical Society, February 10, in Bridgeton Dr. Franklin L. Payne, Philadelphia, discussed "Significance of Abnormal Vaginal Bleeding."

Physicians Honored.—The Summit County Medical Society devoted a recent dinner meeting in Summit to honoring Dr. Thomas P. Prout, who has completed fifty years in the practice of medicine. He was presented with a plaque as a memento of the occasion. Dr. Prout is a founder of the Summit County Medical Society, which was organized in 1905, and also a founder of the Academy of Medicine of Northern New Jersey. In 1902 he established, with the late Dr. Eliot Gorton, the Fair Oaks Sanatorium. He graduated at the College of Physicians and Surgeons, medical department of Columbia College, New York, in 1891.——Dr. George W. Cummins, Belvidere, was guest of honor at a dinner in Belvidere recently given by the Warren County Medical Society to observe his completion of fifty years as a practicing physician. He was presented with honorary life membership in the society. A specially bound volume of Dr. Cummins' book on the medical history of the county was presented to the society by Mrs. Cummins.

NEW YORK

Society News.—The Yonkers Tuberculosis and Public Health Association gave a dinner on Dec. 3, 1941 to mark the twenty-fifth anniversary of its founding; the speakers included Dr. Herbert R. Edwards, director, bureau of tuberculosis, New York City Department of Health, who gave a talk on "The Essential Elements of a Tuberculosis Control Program."——Dr. Herrman L. Blumgart, Boston, discussed angina pectoris before the Medical Society of the County of Albany, January 28.

Fifty Years of Practice.—The Medical Society of the County of Erie recently held its Fall Clinical Day and Dinner to honor physicians who have practiced fifty years or more. The speakers included Drs. Jonathan C. Meakins, Montreal, Canada, from the standpoint of the general practitioner; Charles G. Heyd, New York, "The Concept of Liver Deaths," and Jennings C. Litzenberg, Minneapolis, "Fifty Years of Change in Obstetrics." Dr. Logan Clendening, Kansas City, Mo., was a speaker at the annual dinner, discussing "Reminiscences." There were forty-one guests of honor at the dinner.

Typhoid Carrier Operates Food Store.—A man who had been declared a typhoid carrier in 1937 was recently tried and convicted by a court of special sessions in a community in Westchester County for his failure to keep health officials informed of his whereabouts and to observe other control measures imposed by the state sanitary code. In 1941, after the man had failed to report to district health authorities, an investigation by health and police officials disclosed that the carrier had assumed another name, moved across the street, although friends had reported him to be out of town, and was operating a food store in the immediate neighborhood. In the recent trial he was found guilty of violating the sanitary code, fined $50 and placed on probation for three years.

New York City

Conferences for the Practicing Physician.—The bureau of social hygiene of the city department of health is conducting a series of educational conferences for the physician in practice. The new series opened, February 14, with a conference on "Venereal Diseases for the Practitioner" and will continue on six consecutive Saturday mornings through March 21. Cases from the Central Clinic will be presented, and lectures will be illustrated by lantern slides.

New Society to Consider Psychiatric Problems in Children.—A group of psychiatrists has organized a program to deal with war time psychiatric problems in children. The group has named itself tentatively the New York Society for Child Psychiatry, with temporary headquarters at the Payne Whitney Psychiatric Clinic of New York Hospital. Members of the coordinating committee include Drs. Lauretta Bender, chairman, Juliette Louise Despert, William S. Langford and Frank J. Curran.

Clinic for Speech Disorders.—Plans were recently announced for the establishment of a clinic at the National Hospital for Speech Disorders "for the study of the brain wave patterns of stutterers and sufferers from other speech and voice disorders." According to the New York *Times*, the clinic was to be made possible through grants from Child Neurology Research. Dr. James Sonnett Greene is founder and director of the hospital, which recently celebrated its twenty-fifth anniversary.

OHIO

Hospital News.—The Massillon City Hospital, Massillon, has announced plans to construct a $150,000 addition which will increase its capacity to one hundred and fifty beds. The Office of Dr. William Henry Walsh, Chicago, has been named consultant to prepare plans for the addition.

Society News.—The Montgomery County Medical Society was addressed, February 6, by Dr. Frederick A. Coller, Ann Arbor, Mich., on "Our Water Balance."——The annual meeting of the Cleveland Medical Library Association was addressed, January 6, by Everett Rhodes Castle, humorist and short story writer of Cleveland, on "The Patient Will See You Now, Doctor."

Changes in Health Officers.—Dr. George W. Bassow, Steubenville, has resigned as health commissioner of Jefferson County to return to private practice in Massachusetts.——Dr. Frank Ternocky Jr., Bloomville, has been elected health commissioner of Seneca County.——Dr. Beatrice A. T. Hagen, Zanesville, who has been health commissioner of Muskingum County for twelve years, has been reappointed for a one year term; she is also secretary of the Muskingum County Academy of Medicine.——Dr. Alexander S. Mack, Oak Harbor, has been reappointed health commissioner of Ottawa County.——Dr. Forder F. DeMuth, Hicksville, has been appointed health commissioner of Defiance County, succeeding Dr. Henry C. Lindersmith, Sherwood, resigned.

TENNESSEE

The Flexner Lectures.—The Abraham Flexner Lectures were given at the Vanderbilt University School of Medicine, Nashville, by Drs. Donald D. Van Slyke of the Rockefeller Institute for Medical Research, New York, and Warfield T. Longcope, professor of medicine, Johns Hopkins University School of Medicine, Baltimore. Dr. Van Slyke discussed "Physiology of the Kidney," February 2, and "Renal Function in Diseases of the Kidney," February 3. Dr. Longcope considered "Clinical Nephritis" in both his lectures, February 5 and 6.

Physical Education Program for Public Schools.—The state department of education has set up a five year program for physical education in public schools. It is planned to divide the state into twenty areas, and meetings of school teachers, principals and superintendents will be held to discuss the program. According to an announcement it is proposed to cooperate with all other agencies within the state that have child welfare as an objective to bring about a necessary coordination and correlation of an effective state program. It is also planned to cooperate with the state department of health by adding stimulus to a project of health examination in the public schools of the state which will eventually provide for medical examinations of all pupils in public schools. In a follow-up program, parents will be notified of defects found and urged to refer the child to the family physician for their correction. A well planned program in nutrition, communicable diseases and health instruction is considered in the comprehensive five year project, in which the cooperation of county medical societies, civic and local groups will be enlisted.

TEXAS

Spring Clinical Conference.—The Dallas Southern Clinical Society will hold its fourteenth annual Spring Clinical Conference, March 23-26, at the Hotel Adolphus in Dallas. Guest speakers, each of whom will give more than one paper, will include:

Dr. Tinsley R. Harrison, Winston-Salem, N. C., The Value and Limitation of Drugs in Treatment of Cardiac Disease.
Dr. Lewis M. Hurxthal, Boston, Gastrointestinal Symptoms in Patients with Heart Disease.
Dr. Edward G. Billings, Denver, Differentiation of Psychogenic and Organogenic Gastrointestinal Disorders.
Dr. Alan R. Moritz, Boston, Head Injuries.
Dr. Chester A. Stewart, New Orleans, The Control of Tuberculosis in Private Practice.
Dr. Andrew C. Ivy, Chicago, The Applied Physiology of the Biliary Tract with Therapeutic Considerations.
Dr. George T. Pack, New York, Treatment of Benign and Malignant Tumors of the Skin.
Dr. Barney Brooks, Nashville, Tenn., Operative Treatment for Benign Ulcerations of the Stomach and Duodenum.
Dr. Henricus J. Stander, New York, The Management of Abnormal Vaginal Bleeding.
Dr. Vincent J. O'Conor, Chicago, Urologic Aspect of Low Back Pain.
Dr. Grady E. Clay, Atlanta, Ga., Treatment of Convergent Squint.
Dr. Francis L. Lederer, Chicago, Evaluation of Early Otogenic Complications.

VIRGINIA

Personal.—Dr. Peter A. N. Pastore, Rochester, Minn., has been appointed professor of otolaryngology and rhinology at the Medical College of Virginia, Richmond, where he graduated in 1934.——Dr. and Mrs. James H. Ferguson, Clifton, recently observed their fiftieth wedding anniversary. Dr. Ferguson has also been practicing medicine for fifty years.——Dr. Clifford E. Waller, Silver Spring, Md., medical director, U. S. Public Health Service, retired, has been named health officer in Loudoun County.——Dr. Aaron Wilson Brown, Richmond, recently resigned as full time venereal disease control officer of Richmond to locate in Pocahontas; he was the first to hold this position.

New Division for "General Practice."—The Medical College of Virginia, Richmond, has announced new rules and regulations for the use of private beds in its teaching hospitals. It has been decided to establish a special category for general practice, the latter to cover general medicine, normal obstetrics and lesser surgery. The change is in addition to the present custom of limiting the practice of any accredited member of the staff to one of the major clinical divisions of pediatrics, obstetrics and gynecology, psychiatry and neurology, internal medicine, general surgery and gynecology, and in addition to the usual specialties of medicine and surgery. According to Dr. Lee E. Sutton Jr., dean of the school of medicine, the privilege of practice with private patients in the teaching hospitals is limited to those now on the faculty or to those who have given service under certain conditions in the past.

PUERTO RICO

Congress for the Blind.—The first Pan American Congress of the Blind will be held in Santurce sometime in 1942, the exact date to be announced later. The congress has been organized under the auspices of the Association for the Blind of Puerto Rico. Dr. Jose Pana Reyes is the president of the organizing committee, Apartado 3656, Santurce.

GENERAL

Society News.—The Association of Military Surgeons will hold its 1942 annual session in San Antonio, November 5-7, with headquarters at the Hotel Gunter.——Recently elected officers of the Mississippi Valley Conference on Tuberculosis include Will Ross, Milwaukee, president; Dr. John H. Skavlem, Cincinnati, vice president, and A. W. Jones, St. Louis, secretary-treasurer.

Special Society Election.—Dr. Marius N. Smith-Petersen, Boston, was chosen president-elect of the American Academy of Orthopaedic Surgeons, and Dr. Carl E. Badgley, Ann Arbor, Mich., was installed as president. Other officers are Drs. Robert V. Funsten, Charlottesville, Va., vice president; Philip Lewin, Chicago, librarian; Eugene B. Mumford, Indianapolis, treasurer, and Rex Diveley, Kansas City, Mo., secretary. The next meeting will be in Chicago, Jan. 17-21, 1943.

National Noise Abatement Week.—The National Noise Abatement Council has designated May 31-June 6 as National Noise Abatement Week. Educational efforts this year will be directed to informing the public to a realization of the importance of eliminating needless noise as a vital wartime measure. Preliminary programs are now under consideration in forty principal cities where local noise committees are already formed. Additional information may be obtained from the National Noise Abatement Council, 9 Rockefeller Plaza, New York City.

Examination in Dermatology and Syphilology.—The American Board of Dermatology and Syphilology will hold a written examination in various large cities in the country on November 16. Applications must be received by the secretary on or before October 5. An oral examination will be held in Cleveland on January 14-15, 1943, applications in group A to be received by the secretary, December 7. If sufficient applications are filed before March 23, 1942 an examination will be held at Atlantic City on June 4-5. Dr. Clarence Guy Lane, 416 Marlboro Street, Boston, is the secretary.

Mrs. Emily Cushing Dies.—Mrs. Emily Prescott Cushing, who abstracted foreign medical literature for THE JOURNAL from 1895 until 1926, died February 12 in Belleair, Fla., of cerebral hemorrhage. Mrs. Cushing was born in Tallahassee, Fla., Dec. 31, 1853. She was a member of the Chicago Woman's Club from 1910 to 1928. For a number of years she was responsible for all translations appearing in THE JOURNAL. Mrs. Cushing had facility in translating German, French, Italian, Spanish, the Scandinavian languages, Dutch, Russian, Polish, Portuguese and several local modifications of these languages. She was a prodigious and talented worker.

Conference of Radiologists.—The American College of Radiology held its twelfth annual conference meeting with teachers of clinical radiology, February 15, under the auspices of the Commission on Education at the Palmer House, Chicago. The speakers were Major Sam F. Seeley, Washington, D. C., "The Function of the Procurement and Assignment Service for Physicians, Dentists and Veterinarians"; Major Alfred A. de Lorimier, Washington, D. C., "The Character and Extent of Roentgenological Services in the Field of Combat," and Dr. Joshua C. Dickinson, Tampa, Fla., "What Obligations Do We Have to the Radiologist Who Is Called into the Service?" Dr. Byrl R. Kirklin, Rochester, Minn., led a panel discussion on "Should the Training of Residents and Fellows in Radiology be Modified During the Period of the War?"

Kalamazoo Coaches, Inc., Not Authorized to Mention Approval of Catastrophe Unit.—Dr. George Baehr, chief medical officer, Office of Civilian Defense, Washington, D. C., has written to the effect that the Kalamazoo Coaches, Inc., has not been authorized to mention in its advertising literature that the West Catastrophe Unit is approved by him or by Dr. James M. Macintosh, professor of public health, University of Glasgow and formerly chief health officer of Scotland. Dr. Baehr points out that critical comments made by Professor Macintosh could hardly be considered justification for the statement contained in the advertising literature. In one place he says the vehicle is "too costly for the purpose it serves. . . . Even apart from the expense, I think the principle is wrong. . . . An incident should be regarded as consisting of not less than twenty injured persons. It is obvious that this cramped and costly accommodation could not deal efficiently with this number; time would be wasted at every stage by lack of space and the various boxes containing instruments could not be effectively handled."

Conservation of Scientific Journals.—The Committee on Aid to Libraries in War Areas of the American Library Association has issued an appeal for the conservation of scholarly and scientific journals. The committee believes that timely attention to the fact that libraries in war areas are handicapped in completing their institutional sets of American scholarly, scientific and technical periodicals will obviate a duplication of the difficult task in library reconstruction after the first world war. Many sets of journals will be broken by the financial inability of the institutions to renew subscriptions; many more will have been broken through mail difficulties and loss of shipments; other sets will disappear through destruction of libraries. The committee also points out that, with an imminent paper shortage, attempts are being made to collect old periodicals for pulp and urges that care be shown in the contribution of material to the pulp demand. All communications should be directed to Wayne M. Hartwell, executive assistant, Committee on Aid to Libraries in War Areas, Rush Rhees Library, University of Rochester, Rochester, N. Y.

Southeastern Surgical Congress.—The thirteenth annual postgraduate assembly of the Southeastern Surgical Congress will be held at the Biltmore Hotel, Atlanta, Ga., March 9-11. Special papers to be offered this year in addition to the regular program include the following:

Dr. Fred W. Rankin, Lexington, Ky., The Medical Profession and War Duties.
Dr. Leonard G. Rowntree, chief of the medical division, Selective Service, Washington, D. C., How Can the Medical Profession Augment National Efficiency During Wartime?
Dr. Sanford W. French, Atlanta, Medical and Surgical Service in the Training Camps.
Dr. Robert H. Ivy, Philadelphia, Early and Late Treatment of the Face and Jaws as Applied to War Injuries.
Dr. Joseph D. Collins, Portsmouth, Va., The Part the Railroad Surgeon May Play in the National Emergency.
Dr. James S. McLester, Birmingham, Ala., War and the Nutrition of the Nation.
Dr. Julian L. Rawls, Norfolk, Va., The Medical Profession in the South in Time of War.
Dr. George Baehr, chief medical officer, Office of Civilian Defense, Washington, D. C., Field and Hospital Services for Civilian Casualties.

Mr. Paul V. McNutt, federal security administrator, will also address the meeting.

CANADA

Hospital News.—The Victoria General Hospital, Halifax, Nova Scotia, will construct a new three hundred bed addition. The Office of Dr. William Henry Walsh, Chicago, has been retained as hospital consultant.

Institute of Physiology.—Newspapers reported that the University of Toronto Faculty of Medicine, Toronto, has announced plans to establish an institute of physiology, to be under the direction of Dr. Charles H. Best, professor of physiology and head of the department; also that two new subdepartments have been organized in the School of Hygiene at Toronto; namely, public health administration and nutrition.

LATIN AMERICA

Hygiene Group Formed.—The Asociación Argentina de Médicos Higienistas was recently established in Buenos Aires to project activities now being carried on by centers and groups of hygiene workers and to facilitate all work of hygiene for the public. The association also aims to work for governmental recognition of a "diploma of hygiene physician." Drs. Alfredo Piquero and Juan Pérez del Chaco, Buenos Aires, were chosen president and secretary, respectively. One requirement for membership in the new association is to be approved in the postgraduate course of hygiene which is given by the Institute of Hygiene of the Faculty of Medicine of the University of Buenos Aires.

Deaths in Other Countries

Dr. Heinrich Finkelstein, formerly professor of pediatrics, University of Berlin, Germany, died January 28 at Santiago, Chile, of typhoid complicated by a heart attack. Dr. Finkelstein was born in Leipzig July 31, 1865. He enjoyed an international reputation as a distinguished teacher of pediatrics and was the author of numerous books on his specialty.

Government Services

Proposed Federal Workers Health Service

Newspapers reported on January 30 that plans are being considered to establish a federal workers' health service to reduce sick leave, which costs $100,000,000 a year. Tentatively a unit would be formed in each department, roughly patterned after industrial preventive medicine programs, with the emphasis placed on prevention and discovery of disease. Treatment and cure would be left to the private physician. According to the newspapers, the plan calls for a medical director for each department to be selected from the staff of the U. S. Public Health Service but who would be responsible administratively to the department head. The public health service, through its division of industrial medicine, would coordinate the program. It is proposed that the medical director would perform regular physical examinations to discover disease before it resulted in a request for sick leave, conduct health education programs, discover and remove health hazards, prepare sick leave studies as a basis for improving the medical service and provide first aid and treatment for minor ailments and discomforts.

Health of the Navy

During the calendar year 1940 the general health of the navy was excellent. The principal exception was a major epidemic of influenza, which was widespread from September to December. Also, as was expected, there was a sharp increase of the childhood type of communicable diseases such as measles, mumps and German measles. This was due to the increase of new, unseasoned personnel in the expanding navy. Although these respiratory and other communicable diseases caused a 20 per cent increase in the general admission rate over that of 1939, they were of minor character, averaging only six and eight-tenths sick days per case and causing no increase of death rates. The admission rates for venereal diseases decreased 7 per cent, and for injuries 4 per cent. Seventy-one per cent of the decrease of venereal diseases was due to reduction of syphilis. The general death rate decreased 8 per cent. There were 99,886 new admissions for all causes, giving a rate of 492.99 per thousand as compared with 408.37 in 1939 and 453.16 the previous nine year median. There were 9,643 new admissions for injuries, giving a rate of 47.59 per thousand as compared with 49.38 in 1939 and 60.04 the previous nine year median. There were 392 deaths from all causes, giving a rate of 1.93 per thousand as compared with 2.10 in 1939 and 2.85 the previous nine year median. Motor vehicle accidents caused 85 deaths. There were 32 deaths from drowning. There were 2,907 persons invalided from the service, giving a rate of 14.35 per thousand as compared with 10.37 in 1939 and 12.18 the previous nine year median. The total number of sick days was 1,804,116, giving an average of 8.90 per person and 18.06 per admission. A catastrophe occurred on June 20, 1941, when the submarine U. S. S. 0-9 sank off the Isle of Shoals (Portsmouth, N. H.) while on a trial run. Two officers and thirty-one enlisted men were lost. None were rescued. There were no disasters of major importance during the calendar year 1940.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Jan. 10, 1942.

British Medical Aid to Russia

Mrs. Churchill's Red Cross fund, which in less than two months has raised nearly $5,000,000 for medical help to Russia, is financing the greatest exports of medical and surgical supplies that have ever been sent from this country. Already five large consignments have been sent to Russia, and packages are being dispatched in every ship in which space can be found. The value of the supplies already sent is approximately $1,000,000. The Russian requests are on so vast a scale that it has been possible to supply only a fraction of them. If all the drugs and instruments wanted had been procurable in this country they would have been sent at once. The latest requirements, on which work is proceeding, include twenty-six different drugs in huge quantities and fifty-nine various surgical instruments or requisites in almost astronomical numbers. For example 750,000 ampules of strophanthin and more than 1,600,000 pounds of other drugs are requested. The surgical instruments needed exceed 13,500,000. Britain has been scoured for the articles required, and the Red Cross has bought all it could lay hands on. Large orders are being placed daily and purchases made by the Ministry of Supply through a committee of which the president of the Royal College of Physicians, Sir Charles Wilson, is chairman. He recently visited Russia.

Royal College of Surgeons to Form New Pathologic War Collection

The destruction by German bombs of much of the contents of the great pathologic and anatomic museum formed by the Royal College of Surgeons has been reported in previous letters. The invaluable collection, formed after the last great war, containing plaster casts of every type of wound, was destroyed. Arrangements have been made for the formation of another collection. The Medical Research Council has accepted a request from the War Office and the Royal College of Surgeons that it should assist in the forming of a comprehensive national collection. A special subcommittee of the War Wounds Committee has been appointed for the purpose. This subcommittee includes nominees of the three fighting services, of the Ministry of Health and of the Royal Colleges of Physicians and of Surgeons of London, as well as of the Department of Health for Scotland. It is hoped to secure the cooperation of the whole medical profession in the collection of suitable material. It is proposed that the collection shall include specimens, pictures, photographs and roentgenograms which illustrate the lesions produced by missiles, war gas or explosion gas, secondary missiles, such as fragments of masonry or débris, crushing injuries, the effect of the impact of the blast wave in air or water produced by high explosive detonation, and burns resulting from any of these causes. Material illustrating the mode of repair, the consequences of infection and the results of treatment of war wounds and injuries will be included. Specimens are to be sent in the first place to one of two receiving depots, where they will be classified and temporarily stored.

As the value of any pathologic specimen depends largely on selection, the care taken in collection and the preliminary treatment, general instructions have been given regarding preliminary treatment: 1. Only specimens should be chosen in which the lesions can be clearly displayed. 2. Every care should be taken to maintain the shape and form of the specimen during fixation, when the greatest amount of shrinkage and distortion is liable to occur. A hollow viscus should be packed with absorbent cotton soaked in formaldehyde-saline solution before immersion in the fixative. Structures such as nerves, arteries or slices of solid organs should be fixed on a frame to prevent shrinkage or distortion.

Science and the State

In his presidental address at the two hundred and seventy-ninth anniversary of the Royal Society, Sir Henry Dale, physiologist, dealt with the increased preoccupation of science with the means of waging war and the relations between science and the state. With Russia locked in a struggle for existence and America directing its tremendous scientific and technical potential to the support of the same cause, the diversion of science from its normal objectives had spread round the world. Freedom rather than organization provided the conditions for the highest type of research. Between the two great wars the Royal Society had been given important funds for the support of researches over a wide field, in complete independence of any state control. On the other hand, the remarkable development in this country since 1914 of the state support of research, administered by three advisory councils, had taken place without any obvious detriment to the freedom of science. The Royal Society's function of advising the government had been shared and greatly diminished.

While the existing mechanisms for the support of science by the state were doubtless susceptible of improvement, he found no reason to fear any threat to the freedom of science. But in one direction he had apprehension. If science should become entangled in controversial politics, its freedom might be endangered. If science was allowed to be used as a weapon of political pressure, it could not be protected from the pressure of sectional politics. There would then be danger that fundamental researches having no immediate practical appeal would be neglected or that the rigid standards of true science would be relaxed for propaganda.

Treatment of Malaria in Soldiers

The War Office has issued a pamphlet on the treatment of malaria in soldiers returning from service in malarious areas. The possibility of malaria should be remembered in cases of pyrexia without adequate cause, especially if associated with shivering, vomiting and subsequent sweating, where there has been recent service in a malarious area. Lack of facilities for making an exact diagnosis by microscopic examination of the blood should never cause delay in treatment.

The drugs recommended fall into two groups: (1) antisymptomatic and antipyretic for the acute attack and (2) anti-infective and antirelapse after the acute attack. The antisymptomatic are quinine and mepacrine hydrochloride, the British equivalent of atabrine (German), (atabrine dihydrochloride N. N. R.) and quinacrine (French). The anti-infective drug recommended is pamaquin, the British equivalent of plasmoquine (German). Mepacrine and pamaquin should never be administered concurrently.

The standard army treatment of malaria is as follows:

Days 1 and 2. Quinine bisulfate or hydrochloride, 10 grains (0.65 Gm.) in solution in 1 fluidounce (30 cc.) of water, by mouth thrice in twenty-four hours.

Days 3, 4, 5, 6 and 7. Mepacrine hydrochloride, 0.1 Gm. tablet thrice daily, swallowed whole with a draft of water, after food.

Days 8 and 9. No antimalarial treatment.

Days 10, 11, 12, 13 and 14. Pamaquin, 0.01 Gm. tablet thrice daily after food.

Severe cerebral symptoms may occur, especially in malignant tertian malaria. They require prompt and energetic treatment by intramuscular or intravenous quinine injections. Collapse, possibly with dysenteric symptoms, requires the same treatment. Intravenous quinine should be reserved for cases of great urgency or heavy malignant infection and should never be used as a routine.

Pharmacologic Research

Before the war we depended on Germany for a large number of synthetic drugs. Arrangements have been made for their manufacture in this country to take the place of the German supply, now completely cut off. What appears to be another consequence of the war is stimulation of pharmacologic research. The latest manifestation is the founding by leading drug manufacturers of the Therapeutic Research Corporation of Great Britain, a private limited liability company with an authorized capital of $2,500,000. Its objects are: 1. To coordinate and extend research with a view to accelerating the discovery of new substances for the service of therapeutics and prophylaxis, to ensure collaboration with medical, dental and veterinary practitioners in the introduction of new medicinal substances and to assist in the advancement of medicine by subsidization of research on a broader and more rational basis than has been so far possible in British pharmaceutic industry. 2. To provide for pooling of manufacturing facilities where desirable. 3. To enable industry to cooperate more effectively in national planning by presenting to the government through its appropriate medical, dental, veterinary, scientific and technical organizations the pooled knowledge and facilities acquired in therapeutic research.

The constituent founder companies of the corporation are Boots Drug Company, the British Drug Houses, Glaxo Laboratories, May & Baker and the Wellcome Foundation. Plans for research will be drawn up by a research panel consisting of the heads of research of the constituent companies, which will cooperate or consult with other scientific workers as special problems arise. Products evolved will be sold by the companies under a common name. The corporation will assist wherever practicable in simplifying the nomenclature of new remedies. Its research staffs include many eminent scientific workers.

Honor Memory of Murdered Polish Professors

Leading British scientists and scholars, including Sir William Bragg, lately president of the Royal Society, paid tribute to the memory of the Polish professors murdered by the Germans. The ceremony took place at the Royal Institution, London. Sir David Ross, vice chancellor of the University of Oxford, who presided, said that the persecution of Polish intellectual leaders by the Germans seemed to be part of a deliberate plan to convert Poland into a vassal country of peasants. Prof. Gilbert Murray stated that the Nazis had committed horrors for which ordinary language had no name and were guilty of systematic yet insane wickedness. Prof. Antoni Jurasz, dean of the Polish Medical School formed in Edinburgh, read a long list of names of murdered scientists and addressed them as "Dear colleagues, courageous soldiers in this deadly struggle, let me assure you that your martyrdom shall not be forgotten and that your murderers shall not escape justice."

American Hospital in England

The hospital of the Harvard American Red Cross unit is nearly completed. It consists of twenty-two wooden buildings for which the material required was shipped across the Atlantic in 4 foot sections, with a year's reserve of equipment. The unit has undertaken the study and treatment of epidemic diseases, with particular relation to wartime epidemics. It has sent out mobile field units to camps and other areas where small outbreaks have occurred. The hospital is open to both soldiers and civilians. With the exception of a few British workers, the entire staff is American. There are eight physicians with Dr. J. E. Gordon as director and Dr. Paul Beeson as associate director, and laboratory technicians under Dr. Scott, a dietitian, a chef and more than sixty American graduate nurses. Some twenty-three nurses were torpedoed on the way over and six lost their lives.

BUENOS AIRES

(From Our Regular Correspondent)

Jan. 18, 1942.

Diphtheria Control in Argentina

The antidiphtheric serum which is used in Argentina is prepared by the Bacteriologic Institute of the National Department of Hygiene of Buenos Aires. The reserves of antidiphtheric serum were depleted months ago because of the impossibility of obtaining certain drugs necessary for the preparation and conservation of the serum. A supply of 250,000,000 units of the serum was borrowed from Chile. The situation was controlled shortly after.

The national congress has passed a law for obligatory antidiphtheritic vaccination of all children between 9 months and 2 years of age. By this law the National Department of Hygiene must organize a special department with central and provincial branches for vaccination and revaccination of children. The governors of the provinces will be responsible for the enforcement of the law. The municipal authorities of Buenos Aires and the Council of National Education will cooperate by giving orders to have all school children vaccinated. The vaccine should be given gratis to all children. Parents must permit vaccination of their children. Toxoid as prepared by the Bacteriologic Institute of the National Department of Hygiene and some other vaccines which have been accepted by the national authorities of public health are the only vaccines officially accepted. The vaccine should be administered in only one subcutaneous injection. The immunity should be maintained by revaccination, which should be performed one year after vaccination and again at intervals of three years. All necessary precautions for preventing reactions from hyperallergy are taken. The department of vaccination will give certificates to the parents of the vaccinated children and will keep records of vaccinated and revaccinated children. There are exemptions for children who suffer from diseases which contraindicate vaccination. All cases of suspected diphtheria should be reported to the National Department of Hygiene by writing and within three days by the parents, the directors of schools and the physicians, respectively. The Department of Hygiene will organize several departments for services for resident and semiresident children and also for ambulatory children for the diagnosis of diphtheria and for vaccination. Crusades for sanitary propaganda will be established. Laws for fines and punishment of infractions will be passed. The law will go into effect in July 1942.

Brief Items

According to a report of the ministry for public health in Paraguay, a Rockefeller research group which works in Matto Grosso, Brazil, will conduct scientific investigations on yellow fever transmitting mosquitoes in the region of the Rio Paraguay.

The Uruguayan minister for public health, Prof. Juan César Mussio Fournier, attended the meeting of the Public Health Association held in Atlantic City in October.

In response to an invitation, the Argentine government has formed a committee which is to organize the participation of Argentina in the eighth Pan American Congress of the Child (Washington, 1942); Prof. Gregorio Aráoz Alfaro is chairman.

Marriages

JOHN WINSLOW HIRSHFELD, Detroit, to Miss Barbara Elizabeth Babcock in Ithaca, N. Y., in December 1941.

JAMES FRANKLIN REINHARDT, Lincolnton, N. C., to Miss Jane Washburn of Shelby in December 1941.

SAMUEL GENDELMAN, Manchester, Ohio, to Miss Betty Williams of Charleston, S. C., January 8.

Deaths

Stewart Paton, Baltimore; College of Physicians and Surgeons, medical department of Columbia College, New York, 1889; member of the Medical and Chirurgical Faculty of Maryland, American Neurological Association, Association for Research in Nervous and Mental Disease and the American Psychopathological Association; formerly associate in psychiatry at the Johns Hopkins University, lecturer in neurobiology at Princeton (N. J.) University and in psychiatry at his alma mater; was consultant in mental hygiene and lecturer in psychiatry at Yale University, New Haven, Conn., from 1926 to 1928; at one time director of the laboratory of the Sheppard and Enoch Pratt Hospital; trustee of the Carnegie Institution of Washington; author of "Psychiatry," "Education in Peace and War," "Human Behavior," "Signs of Sanity and the Principles of Mental Hygiene" and "Prohibiting Minds and the Present Social and Economic Crisis"; aged 76; died, January 7, of heart disease.

Sidney Johnston Wilson ✠ Fort Worth, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1906; past president of the Tarrant County Medical Society and the North Texas District Medical Society; member of the American Academy of Dermatology and Syphilology; professor of dermatology at the Texas Christian University Medical Department from 1912 to 1917; served in various capacities on the staffs of Baptist Hospital, City and County Hospital, Children's Hospital, Methodist Hospital and All Saints Episcopal Hospital; served during the World War; aged 59; died, Dec. 23, 1941, of coronary occlusion.

John Blair Kessler, Cedar Rapids, Iowa; State University of Iowa College of Medicine, Iowa City, 1877; Bellevue Hospital Medical College, New York, 1883; member of the Iowa State Medical Society; vice chairman of the Section on Dermatology of the American Medical Association, 1914-1915; at various times instructor and professor of dermatology and since 1933 emeritus professor of dermatology and syphilology at his alma mater; was pension examiner of the United States; formerly member of the Johnson County Insane Commission; aged 91; died, January 14, of arteriosclerosis and myocarditis.

Hugh De Valin ✠ Medical Director, United States Public Health Service, retired, New Orleans; University of Pennsylvania Department of Medicine, Philadelphia, 1899; became an assistant surgeon in the United States Public Health Service Aug. 30, 1905, a passed assistant surgeon Sept. 16, 1909, surgeon, Dec. 20, 1917, senior surgeon July 1, 1930 and medical director, Sept. 5, 1931; retired in 1939; aged 69; died, February 3, in the United States Marine Hospital of pneumonia.

Francis Joseph Scanlan, Johnstown, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1929; member of the Medical Society of the State of Pennsylvania; in 1936 was appointed to the Municipal Civil Service Commission for police and served as chairman of the board until his retirement in 1940; president of the Lee Homeopathic Hospital and in charge of the pediatrics department; aged 39; died at home, Dec. 2, 1941, of coronary thrombosis.

John Francis Urie ✠ Surgeon, Lieutenant Commander, United States Navy, retired, New London, Conn.; Harvard Medical School, Boston, 1888; entered the navy in 1888 and retired Aug. 1, 1908 for incapacity resulting from an incident of service; recalled to active duty on Sept. 15, 1917 as commanding officer, U. S. Naval Hospital, U. S. Naval Station, New Orleans; retired from active duty in May 1919; aged 79; died, January 8, of coronary thrombosis.

Frank W. Kenney, Denver; University of the City of New York Medical Department, 1893; member of the Colorado State Medical Society; served during the World War; consultant, St. Luke's Hospital, Children's Hospital and the Denver General Hospital; associate, Presbyterian Hospital, St. Anthony Hospital and St. Joseph's Hospital; medical director of the Capitol Life Insurance Company; aged 81; died, Dec. 19, 1941, of carcinoma of the prostate.

Robert T. Barnett, Lewistown, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1895; member of the Medical Society of the State of Pennsylvania; past president of the Mifflin County Medical Society, for many years a member of the board of health; formerly member of the board of education; on the staff of the Lewistown Hospital; aged 68; died, Dec. 30, 1941, of coronary thrombosis.

Walter Cox Barker, Philadelphia; Hahnemann Medical College and Hospital of Philadephia, 1903; member of the Medical Society of the State of Pennsylvania, American Roentgen Ray Society, Radiological Society of North America, Inc., and the American College of Radiology; on the staff of the Broad Street Hospital; aged 63; died, Dec. 27, 1941, at his home in Wynnefield of cerebral thrombosis.

Charles A. Greer, Oglethorpe, Ga.; Louisville (Ky.) Medical College, 1892; member of the Medical Association of Georgia; past president of the Macon County Medical Society; secretary-treasurer of the Third District Medical Society; for many years mayor; served in the lower and upper houses of the General Assembly of Georgia; aged 68; died, Oct. 9, 1941, of coronary occlusion.

William Frederick Zierath, Sheboygan, Wis.; Northwestern University Medical School, Chicago, 1904; member of the board of trustees of the Rocky Knoll Sanatorium from August 1926 to Dec. 31, 1931 and again from Jan. 1, 1936 until his death; aged 64; died, Dec. 5, 1941, of chronic myocarditis, paralysis agitans and bronchopneumonia.

Philip Worcester Bill, Westport, Conn.; Columbia University College of Physicians and Surgeons, New York, 1901; member of the Connecticut State Medical Society; fellow of the American College of Surgeons; member of the honorary consulting staff of the Bridgeport Hospital; aged 67; died, Dec. 29, 1941, of coronary thrombosis.

Frederick Eugene McCarty, Wellsville, N. Y.; University of Buffalo School of Medicine, 1915; served during the World War; past president of the Allegany County Medical Society; aged 48; died, January 10, of cirrhosis of the liver in the Memorial Hospital of William F. and Gertrude F. Jones, where he was a member of the staff.

Carl White Jones, High Point, N. C.; Jefferson Medical College of Philadelphia, 1937, was appointed resident in obstetrics and gynecology, New York Lying-In Hospital, New York, for 1942-1943; aged 29; died, Dec. 24, 1941, in the Baptist Hospital, Winston-Salem, of pulmonary embolus complicating staphylococcic bronchial pneumonia.

Charles S. Austin ✠ Carrollton, Mo.; Missouri Medical College, St. Louis, 1887; president of the Carroll County Medical Society; formerly county and city health officer; at one time county coroner; since 1928 member of the board of curators of Central College, Fayette; aged 79; died, Dec. 18, 1941, of carcinoma of the liver.

Victor E. Potvin, Claremont, N. H.; Laval University Medical Faculty, Montreal, Que., Canada, 1909; member of the New Hampshire Medical Society; past president of the Sullivan County Medical Society; formerly bank president; on the staff of the Claremont Hospital; aged 56; died, Dec. 10, 1941, of heart disease.

Edmund Channing Stowell ✠ Marlboro, N. H.; Harvard Medical School, Boston, 1892; member of the Massachusetts Medical Society; instructor of children's diseases from 1895 to 1900 and assistant professor from 1900 to 1911 at Tufts College Medical School, Boston; aged 75; died, Dec. 20, 1941, of heart disease.

Charles Louis Mosley, Fort Scott, Kan.; Barnes Medical College, St. Louis, 1908 and 1909; member of the Kansas Medical Society; served during the World War; was health officer of Fort Scott; aged 55; on the staff of the Mercy Hospital where he died, Dec. 2, 1941, of carcinoma of the left lung.

Frank Flanneghan Davis, East Liverpool, Ohio; Homeopathic Hospital College, Cleveland, 1896; member of the Ohio State Medical Association; served during the World War; aged 66; died, Dec. 19, 1941, in the Veterans Administration Facility, Aspinwall, Pa., of hypertension and coronary sclerosis.

Louise Tayler Jones ✠ McLean, Va.; Johns Hopkins University School of Medicine, Baltimore, 1903; member of the Medical Society of the District of Columbia; fellow of the American College of Physicians; aged 71; died, Dec. 21, 1941, of carcinoma of the breast with metastases to the lung.

Francis Alexander Thompson ✠ Milwaukee; Wisconsin College of Physicians and Surgeons, Milwaukee, 1897; assistant clinical professor of medicine at the Marquette University School of Medicine; served during the World War; aged 68; died, January 7, of coronary thrombosis.

Samuel Cathcart Ketchin, Louisville, Ga.; Medical College of the State of South Carolina, Charleston, 1916; member of the Medical Association of Georgia; served during the World War; county health officer; aged 50; died, Dec. 22, 1941, of coronary occlusion.

John G. Clay, Dallas, Texas; Vanderbilt University School of Medicine, Dallas, Texas, 1882; University of Nashville (Tenn.) Medical Department, 1883; aged 83; died in November 1941 of pneumonia, enlarged prostate with urinary obstruction and uremia.

Edward Lingan Bowlus, Baltimore; University of Maryland School of Medicine, Baltimore, 1906; pathologist, Hospital for the Women of Maryland from 1925 to 1928; aged 69; died, Dec. 31, 1941, in St. Joseph's Hospital of arteriosclerosis.

Howard Spaulding Ballard, McKeesport, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1903; formerly on the staff of the McKeesport Hospital; aged 62; died, Dec. 27, 1941, of injuries received in an automobile accident.

William Herbert Gorton MacKay, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1907; member of the Medical Society of the State of Pennsylvania; served during the World War; aged 58; died, January 5.

Corles Belford Cline, Saybrook, Ill.; Eclectic Medical Institute, Cincinnati, 1897; for many years mayor of Saybrook; aged 69; died, Dec. 31, 1941, in the Mennonite Hospital, Bloomington, of endarteritis obliterans secondary to endocarditis.

John Walker Croft, Waynesboro, Pa.; Jefferson Medical College of Philadelphia, 1899; member of the Medical Society of the State of Pennsylvania; on the staff of the Waynesboro Hospital; aged 67; died, Dec. 24, 1941, of coronary occlusion.

Bodog Felix Beck, New York; Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest, Hungary, 1894; author of "Honey and Health" and "Bee Venom Therapy"; aged 73; died, January 1, of chronic myocarditis.

Simeon E. Mentzer ✠ Monroeville, Ind.; Medical College of Ohio, Cincinnati, 1885; Bellevue Hospital Medical College, New York, 1894; aged 79; died, January 11, in the Lutheran Hospital, Fort Wayne, of carcinoma of the right lung.

George Lawrence Sandy, Martinsville, Ind.; Indiana University School of Medicine, Indianapolis, 1931; on the staff of the Central State Hospital, Indianapolis; aged 41; died, Dec. 18, 1941, of injuries received in an automobile accident.

Edward John Jenkins, Glen Gardner, N. J.; Jefferson Medical College of Philadelphia, 1933; resident, New Jersey Sanatorium for Tuberculous Diseases; aged 34; died, Dec. 30, 1941, of pulmonary, laryngeal and enteric tuberculosis.

James Eugene Davies, Oxford Junction, Iowa; St. Louis College of Physicians and Surgeons, 1898; member of the Iowa State Medical Society; aged 68; died, Dec. 26, 1941, in a hospital at Maquoketa of cerebral hemorrhage.

Bertie Virgil Swisher, Radcliff, Ohio; Cincinnati College of Medicine and Surgery, 1901; served as a member and president of the Vinton County District Board of Health; aged 67; died, Dec. 15, 1941, of cerebral hemorrhage.

Felix Reville Brunot ✠ Surgeon, United States Public Health Service, Bethesda, Md.; Tulane University of Louisiana School of Medicine, New Orleans, 1920; aged 47; died, January 4, of a self-inflicted bullet wound.

Daniel Beckel Conklin ✠ Dayton, Ohio; Columbia University College of Physicians and Surgeons, New York, 1902; past president of the city board of health; aged 64; died, Dec. 13, 1941, of cerebral hemorrhage.

Herman Clyde Hughes, Du Bois, Pa.; Jefferson Medical College of Philadelphia, 1912; member of the staffs of the Maple Avenue and Du Bois hospitals; aged 62; died, Dec. 26, 1941, of cardiovascular renal disease.

Herbert John Schmoyer ✠ Bethlehem, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1905; on the staff of St. Luke's Hospital; aged 64; died, Dec. 15, 1941, of coronary occlusion.

Joseph Andrew Chapman, Bakersfield, Calif.; University of Texas School of Medicine, Galveston, 1924; member of the California Medical Association; aged 43; died, Nov. 15, 1941, of cirrhosis of the liver.

James William Salisbury, Toledo, Ohio; Eclectic Medical Institute, Cincinnati, 1897; aged 70; died, Dec. 17, 1941, in the Veterans Administration Facility, Dearborn, Mich., of congestive heart disease.

Robert B. Longmire, Hale Center, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1882; aged 80; died, Dec. 19, 1941, in a hospital at Plainview of cerebral hemorrhage.

Manley Forsythe, Fremont, Iowa; Keokuk Medical College, College of Physicians and Surgeons, 1908; member of the Iowa State Medical Society; aged 62; died, Dec. 16, 1941, of cerebral hemorrhage.

Christopher C. Howard, Topeka, Kan.; Medico-Chirurgical College of Kansas City, Mo., 1905; formerly a minister; aged 82; died, January 2, of angina pectoris, chronic myocarditis and arteriosclerosis.

William A. Shobe, Ligonier, Ind.; Detroit Medical College, 1880; member of the Indiana State Medical Association; aged 85; died, Dec. 18, 1941, of carcinoma of the liver with metastases.

Oscar Johnson, Pike Road, Ala.; Medical College of Alabama, Mobile, 1896; member of the Medical Association of the State of Alabama; aged 75; died, Dec. 17, 1941, of senility.

George Curtis Lyon ✠ Longview, Texas; Atlanta (Ga.) School of Medicine, 1906; aged 63; died, Dec. 16, 1941, in the Tri-State Hospital, Shreveport, La., of coronary thrombosis.

Henry W. Heuser, Louisville, Ky.; Hospital College of Medicine, Louisville, 1900; aged 76; died, January 10, in St. Anthony's Hospital of a skull fracture received in a fall.

Winthrop Clinton Lincoln, Providence, R. I.; Boston University School of Medicine, 1909; served during the World War; aged 75; died, Dec. 16, 1941, of coronary occlusion.

Clara L. Kembel Cronk, Bloomfield, Iowa; Keokuk Medical College, 1892; member of the Iowa State Medical Society; aged 78; died, Dec. 19, 1941, of coronary thrombosis.

Julius John Jeude, St. Louis; Missouri Medical College, St. Louis, 1898; aged 65; died, January 11, in the Lutheran Hospital of pyloric obstruction due to gastric ulcer.

Colin G. Robertson ✠ Sandusky, Mich.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1901; aged 66; died, Dec. 19, 1941, of coronary thrombosis.

Reginald Franklin Grant, San Francisco; College of Physicians and Surgeons, Los Angeles, 1921; aged 57; died, Dec. 26, 1941, of cardiac decompensation.

Hugh M. McCullough, Louisville, Ky.; University of Louisville Medical Department, 1878; formerly county coroner; aged 83; died, January 8, of myocarditis.

James Gilmer Stone ✠ Bloomfield, Iowa; Hahnemann Medical College and Hospital, Chicago, 1908; aged 58; died, Dec. 15, 1941, of cerebral hemorrhage.

Wesley Franklin Stoneburner, Akron, Ohio; Starling Medical College, Columbus, 1898; aged 68; died, Dec. 14, 1941, in Los Angeles of bronchopneumonia.

Harry John Krudop, Mobile, Ala.; Medical College of Alabama, Mobile, 1904; aged 70; died, Dec. 17, 1941, of myocarditis and cirrhosis of the liver.

Rodolfo Z. Pereyra, El Paso, Texas; Escuela Médico Militar, México, D. F., 1919; aged 49; died, Dec. 9, 1941, in Cuernavaca, Mexico, of myelitis.

Mark Harpel Cornish, Sharon Hill, Pa.; Hahnemann Medical College and Hospital of Philadephia, 1894; aged 73; died, Dec. 18, 1941, of uremia.

Frederick Archimedes Korell, Columbus, Ohio; Starling Medical College, Columbus, 1892; aged 80; died, Dec. 19, 1941, of a self-inflicted bullet wound.

Isaac Newton Simpers, Gaithersburg, Md.; Baltimore Medical College, 1891; aged 73; died, Dec. 28, 1941, of heart disease and nephritis.

J. Barrett Kleckner, Lynchburg, Ohio; American Medical College, St. Louis, 1883; aged 89; died, Dec. 19, 1941, of cerebral hemorrhage.

Thomas Benton Miller, Butler, N. J.; Jefferson Medical College of Philadelphia, 1910; aged 67; died, Dec. 17, 1941, of cerebral thrombosis.

Rollin Stephen Gregory, Portland, Ore.; Denver Homeopathic College, 1899; aged 77; died in November 1941 of carcinoma of the foot.

Marion Grant Wyatt, Bartlesville, Okla.; Missouri Medical College, St. Louis, 1884; aged 77; died, Dec. 29, 1941, of pneumonia.

Joseph Bedford Hix ✠ Altus, Okla.; University of Nashville (Tenn.) Medical Department, 1909; aged 63; died, Dec. 13, 1941.

Arthur Thomas Hudson, St. Petersburg, Fla.; Barnes Medical College, St. Louis, 1898; aged 69; died, January 2.

George Jacob Weitz, Cleveland; Medical College of Indiana, Indianapolis, 1898; aged 65; died, Dec. 12, 1941.

Council on Medical Education and Hospitals

ACCELERATION OF MEDICAL COURSE

Resolution Adopted by the Council on Medical Education and Hospitals of the American Medical Association Meeting at the Palmer House in Chicago, Feb. 15, 1942

The Council is of the opinion that the adoption of a program for an accelerated curriculum for approved medical schools during this war period is a decision which should be determined by each medical school.

The decision of a medical school to initiate an accelerated curriculum should be made only after a comprehensive survey of the personnel, facilities and equipment of the school and its ability to give a medical education without deterioration of the quality of the medical instruction and in conformity with the statutes of the various states and the rulings of the state medical boards.

The Council stands ready to make necessary inspections whenever in its judgment such inspections are required to maintain the present high standards of medical education.

The Council believes that financial assistance for needy medical students during the accelerated program is best provided through scholarships or loans.

UNIVERSITY OF GEORGIA SCHOOL OF MEDICINE DROPPED FROM APPROVED LIST

At its business meeting in Chicago on February 15 the Council on Medical Education and Hospitals of the American Medical Association voted as follows:

Resolved, That the University of Georgia School of Medicine be dropped from the approved list of medical schools of the Council on Medical Education and Hospitals without prejudice to the students enrolled as of Sept. 1, 1942.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and Examining Boards in Specialties were published in THE JOURNAL, February 21, page 665.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 16-18. Acting Sec., Dr. B. F. Austin, 519 Dexter Ave., Montgomery.

ARIZONA: * Phoenix, April 7-8. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

ARKANSAS: * *Medical.* Little Rock, June 4-5. Sec., Dr. D. L. Owens, Harrison. *Eclectic.* Little Rock, June 4-5. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Written.* Los Angeles, March 2-5. *Oral examination* (required when reciprocity application is based on a state certificate or license issued ten or more years before filing application in California), San Francisco, March 18. Sec., Dr. Charles B. Pinkham, 1020 N St., Sacramento.

COLORADO: * *Endorsement.* Denver, April 7. *Examination.* Denver, April 8-10. Application must be on file not later than March 21. Sec., Dr. George R. Buck, 831 Republic Bldg., Denver.

CONNECTICUT: * *Medical. Examination.* Hartford, March 10-11. *Endorsement.* Hartford, March 24. Sec. to the Board, Dr. Creighton Barker, 258 Church St., New Haven. *Homeopathic.* Derby, March 10-11. Sec., Dr. Joseph H. Evans, 1488 Chapel St., New Haven.

DELAWARE: Dover, July 14-16. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

FLORIDA: * Jacksonville, June 22-23. Sec., Dr. William M. Rowlett, Box 786, Tampa.

GEORGIA: Atlanta, June. Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

ILLINOIS: Chicago, April 7-9. Superintendent of Registration, Mr. Philip M. Harman, Department of Registration and Education, Springfield.

INDIANA: Indianapolis, June 16-18. Sec., Board of Registration and Examination, Dr. J. W. Bowers, 301 State House, Indianapolis.

KANSAS: Kansas City, June 2-3. Sec., Board of Medical Registration and Examination, Dr. J. F. Hassig, 905 N. Seventh St., Kansas City.

KENTUCKY: Louisville, May 27-29. Sec., State Board of Health, Dr. A. T. McCormack, 620 S. Third St., Louisville.

MAINE: Portland, March 10-11. Sec., Board of Registration of Medicine, Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Medical.* Baltimore, June 9-12. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. *Homeopathic.* Baltimore, June 16-17. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MASSACHUSETTS: Boston, March 10-13. Sec., Board of Registration in Medicine, Dr. Stephen Rushmore, 413-F State House, Boston.

MICHIGAN: * Ann Arbor and Detroit, June 10-12. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 202-4 Hollister Bldg., Lansing.

MINNESOTA: * Minneapolis, April 21-23. Sec., Dr. Julian F. Du Bois, 230 Lowry Medical Arts Bldg., St. Paul.

MISSISSIPPI: Jackson, June. Assistant Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MONTANA: Helena, April 7-8. Sec., Dr. Otto G. Klein, First National Bank Bldg., Helena.

NEW HAMPSHIRE: Concord, March 12-13. Sec., Dr. T. P. Burroughs, Board of Registration in Medicine, State House, Concord.

NEW JERSEY: Trenton, June 16-17. Sec., Dr. Earl S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * Santa Fe, April 13-14. Sec., Dr. Le Grand Ward 135 Sena Plaza, Santa Fe.

NORTH CAROLINA: Raleigh, June 15. Sec., Dr. W. D. James, Hamlet.

NORTH DAKOTA: Grand Forks, July 7-10. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OHIO: *Endorsement.* April 7. *Written.* Columbus, June. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA: * Oklahoma City, June 10-11. Sec., Dr. James D. Osborn, Jr., Frederick.

OREGON: * Portland, April 7. Exec. Sec., Miss Lorienne M. Conlee, 608 Failing Bldg., Portland.

PENNSYLVANIA: Philadelphia and Pittsburgh, July. Act. Sec., Bureau of Professional Licensing, Mrs. Marguerite G. Steiner, 358 Education Bldg., Harrisburg.

RHODE ISLAND: * Providence, April 2-3. Chief, Division of Examiners, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

TEXAS: Galveston, March 23-25. Sec., Dr. T. J. Crowe, 918-20 Texas Bank Bldg., Dallas.

UTAH: Salt Lake City, June 29-30. Assistant Dir., Department of Registration, Mr. G. V. Billings, 324 State Capitol Bldg., Salt Lake City.

VIRGINIA: Richmond, June 17-20. Sec., Dr. J. W. Preston, 30½ Franklin Rd., Roanoke.

WEST VIRGINIA: Charleston, March 2-4. Commissioner, Public Health Council, Dr. C. F. McClintic, State Capitol, Charleston.

WISCONSIN: * Milwaukee, June 30-July 3. Sec., Dr. H. W. Shutter, 425 E. Wisconsin Ave., Milwaukee.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: Tucson, March 17. Sec., Mr. Franklin E. Roach, Science Hall, University of Arizona, Tucson.

COLORADO: Denver, March 10-11. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver.

DISTRICT OF COLUMBIA: Washington, April 20-21. Sec., Commission on Licensure, Dr. George C. Ruhland, 6150 E. Municipal Bldg., Washington.

FLORIDA: Gainesville, June 8. Sec., Professor J. F. Conn, John B. Stetson University, De Land.

IOWA: Des Moines, April 14. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

MINNESOTA: Minneapolis, April 7-8. Sec., Dr. J. C. McKinley, 126 Millard Hall, University of Minnesota, Minneapolis.

NEBRASKA: Omaha, May 5-6. Dir., Bureau of Examining Boards, Mrs. Jeannette Crawford, 1009 State Capitol Bldg., Lincoln.

OKLAHOMA: Oklahoma City, May 15. Sec., Dr. Oscar C. Newman, Shattuck.

OREGON: Corvallis, July 11. Sec., Mr. Charles D. Byrne, University of Oregon, Eugene.

SOUTH DAKOTA: Vermillion, June 5-6. Sec., Dr. G. M. Evans, Yankton.

WISCONSIN: Madison, April 11. Sec., Prof. Robert N. Bauer, 152 W. Wisconsin Ave., Milwaukee.

Oregon December Report

The Oregon State Board of Medical Examiners reports 4 physicians licensed to practice medicine by reciprocity from Oct. 16 through Dec. 9, 1941. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Northwestern University Medical School		(1937)	Utah
University of Alberta Faculty of Medicine		(1940)	Canada
University of Toronto Faculty of Medicine		(1936)	Canada
Osteopath *			Kansas

* Licensed to practice surgery.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Alleged Negligence in Treatment of Infection of Foot Following Piercing of Sole by Nail.—On May 26, 1934, when Angelina Sales, a woman aged 26, was seven months pregnant, a nail in her shoe pierced the sole of her foot. She bathed the foot in a warm water and lysol solution. The injury did not bother her during the next few days and on May 30 she even took a long walk. The next day she felt a pain "which seemed to shoot upward" from her foot and noticed a pimple on the top of her foot directly over the place that the nail had pierced the sole. She burned the point of a needle with a match, pricked the pimple and soaked the foot in a lysol solution. Later in the day the pain became more severe and the defendant physician was called, arriving about 9 o'clock in the evening. He noted a "dark red, hot area . . . about the size of a 50 cent piece," and the presence of some pus and swelling in the foot. He failed to take her temperature but advised soaking the foot in warm water and epsom salt for twenty minutes every two hours. According to the physician, there was no localized abscess at that time. The treatment advised by the physician was followed, but the pain grew worse and the redness became darker, spreading from the ankle higher up the leg. Two telephone calls were made to the defendant during the early morning hours of June 1 and he advised continuance of the treatment he had prescribed. He visited the patient at 6 a. m., at which time the foot was more discolored and the red area extended up the leg. He "prescribed a wash solution and opiates" and again at 8 o'clock, apparently by phone, recommended that the same treatments be followed. At 10:30 he returned with Dr. Caglieri, who observed that the foot was badly swollen and discolored and suggested that it be placed in a high position, but he saw no necessity for an incision. Although the defendant indicated an intention to hospitalize the patient immediately and ordered an ambulance, it was 2 p. m. before she was taken to a hospital. In the meantime, about 1:30, in the absence of medical attention, the patient delivered, the child dying shortly thereafter. When the patient was received at the hospital, she was in great pain, her foot was discolored and badly swollen and the redness ran high up her leg. Hospital physicians found "infection, early gangrene and chain streptococci." According to these physicians "there was no evidence of an abscess or localization of pus but . . . the infection was general and hence there was no need for an incision." According to one of these physicians, the patient at that time had cellulitis of the foot. The following day, June 2, "a guillotine amputation" of the leg was performed.

Subsequently the patient and her husband brought suit for malpractice against the physician, basing their claim of malpractice apparently on the failure of the defendant to drain the point of infection. Several medical witnesses called by the defendant testified that there was no localized abscess of any kind, that the infection was general, that there would be no reason to make an incision and that the customary treatment was wet heat, such as the defendant had prescribed. A pathologist, who made a laboratory examination of the amputated foot, testified that he found no evidence of an abscess in the foot at that time and that if there had been an abscess in the foot on the defendant's first call some evidence of it must have persisted to the time of amputation. Apparently only one medical witness testified on behalf of the plaintiffs. This physician, in answer to a hypothetical question, stated that when the defendant first called on the patient there was an abscess present in the foot and that in the exercise of that degree of care and skill ordinarily possessed and exercised by physicians and surgeons in San Francisco (the city in which the plaintiff lived and in which the defendant physician practiced) "the only method of choice (was) the prompt opening of the primary point of infection, draining the point of infection under antiseptic methods, and by local anesthesia." He further gave it as his opinion that the infection was afterward generalized, spreading up the leg through the system, that this resulted in the loss of the baby and the necessity for the amputation, and that these would not have occurred if the abscess had been promptly opened and drained. There was a judgment in favor of the plaintiffs and the defendant physician appealed to the district court of appeal, first district, division 2, California.

Apparently the only medical witness testifying on behalf of the plaintiffs practiced in Oakland and had never practiced in San Francisco. The defendant accordingly contended that that physician was not qualified to testify as to the method customarily used to treat such an infection in San Francisco. In view of the close proximity of the two cities, said the appellate court, and the metropolitan character of the entire area, under the circumstances this witness was sufficiently qualified to testify. This witness's testimony created a conflict in the evidence and is sufficient to support the verdict of the jury. The testimony of a medical witness in answer to a hypothetical question based on the facts in the record is sufficient to support a finding contrary to the testimony of all other medical witnesses who have seen and examined the patient. Nor can the fact that the testimony of the medical witness called by the plaintiffs conflicted with all the other medical testimony affect this rule, since the testimony of one credible witness, if believed by the jury, is sufficient to support a verdict.

The court further held that the question as to the patient's contributory negligence in treating her foot as she did before calling the defendant physician was for the jury's valuation and that the plaintiffs' medical witness's testimony supported the finding that the defendant physician's negligent treatment was the proximate cause of the serious results that followed.

The plaintiffs' medical witness was asked on cross examination if during prohibition his federal license to prescribe liquors had not been revoked. He answered: "No." The defendant then attempted to introduce a certified copy of an order revoking this license. The trial court, said the appellate court, properly sustained an objection to this. The credibility of the witness could not be attacked by evidence of specific wrong doing, if this could be so construed, and, the inquiry having been directed to a collateral matter, the defendant was bound by the witness's answer.

The judgment in favor of the plaintiffs was accordingly affirmed.—*Sales v. Bacigalupi, 117 P. (2d) 399 (Cal., 1941).*

Society Proceedings

COMING MEETINGS

Alabama, Medical Association of the State of, Montgomery, Apr. 21-23. Dr. D. L. Cannon, 519 Dexter Avenue, Montgomery, Secretary.

American Association of Anatomists, New York, April 1-3. Dr. Eliot R. Clark, Dept. of Anatomy, University of Pennsylvania School of Medicine, Philadelphia, Secretary.

American Association of Industrial Physicians and Surgeons, Cincinnati, Apr. 13-17. Dr. Edward C. Holmblad, 28 East Jackson Blvd., Chicago, Managing Director.

American Association of Pathologists and Bacteriologists, St. Louis, April 2-3. Dr. Howard T. Karsner, 2085 Adelbert Rd., Cleveland, Secretary.

American College of Physicians, St. Paul, Apr. 20-24. Mr. E. R. Loveland, 4200 Pine St., Philadelphia, Executive Secretary.

American Federation for Clinical Research, Minneapolis, Apr. 20-21. Dr. Thomas M. Durant, 3401 North Broad St., Philadelphia, Secretary.

American Physiological Society, Boston, March 30-April 4. Dr. Carl J. Wiggers, 2109 Adelbert Rd., Cleveland, Secretary.

American Society for Experimental Pathology, Boston, April 1-3. Dr. Harry P. Smith, Medical Laboratory Bldg., Iowa City, Secretary.

American Society for Pharmacology and Experimental Therapeutics, Boston, March 31-April 4. Dr. Raymond N. Bieter, University of Minnesota Medical School, Minneapolis, Secretary.

American Society of Biological Chemists, Boston, Apr. 7. Dr. A. K. Balls, Bureau of Agricultural and Engineering Chemistry, Washington, D. C., Secretary.

American Surgical Association, New Orleans, Apr. 6-8. Dr. Charles G. Mixter, 319 Longwood Ave., Boston, Secretary.

Federation of American Societies for Experimental Biology, Boston, March 31-April 4. Dr. D. R. Hooker, 19 West Chase St., Baltimore, Secretary.

Florida Medical Association, Palm Beach, Apr. 13-15. Dr. Shaler Richardson, 111 West Adams St., Jacksonville, Secretary.

Iowa State Medical Society, Des Moines, Apr. 15-17. Dr. Robert L. Parker, 3510 Sixth Ave., Des Moines, Secretary.

New Jersey, Medical Society of, Atlantic City, Apr. 21-23. Dr. Alfred Stahl, 55 Lincoln Park, Newark, Secretary.

Tennessee State Medical Association, Memphis, Apr. 14-16. Dr. H. H. Shoulders, 706 Church St., Nashville, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1932 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Iowa State Medical Society Journal, Des Moines

31:563-618 (Dec.) 1941

Certain Considerations of Coronary Disease. F. A. Willius, Rochester, Minn.—p. 563.
Significant X-Ray Findings in Heart Disease. H. C. Bone, Des Moines.—p. 569.
Hypersensitiveness of Conjunctiva and Cornea: Report of Case. H. C. Kluever, C. H. Coughlan and L. M. Martin, Fort Dodge.—p. 572.
*Relation of Thyroid Gland to Menstrual Bleeding. R. M. Collins, Council Bluffs.—p. 576.
Diagnosis of Gallbladder Disease. E. H. Sibley, Sioux City.—p. 578.
Practical Application of Obstetric Analgesia. C. W. Seibert, Waterloo.—p. 583.
Decreasing Mortality Rate of Appendicitis. F. W. Mulsow, Cedar Rapids.—p. 585.

The Thyroid and Menstrual Bleeding.—Collins points out that thyroid is indicated for the patient with a slightly subnormal basal metabolic rate who has menstrual disorders, sterility and the likelihood of abortion but that if the rate is slightly elevated compound solution of iodine is indicated. The menstrual and general symptoms in the two types of patient may be identical. In patients with menorrhagia, amenorrhea, dysmenorrhea, sterility and tendency to abortion, hypothyroidism prevails but hyperthyroidism is not uncommon.

Journal of Nervous and Mental Disease, New York

94:669-796 (Dec.) 1941

Monstrosity Due to Intrauterine Purulent Meningoencephalitis. H. N. Roback, Cuyahoga Falls, Ohio, and H. F. Kahler, Medical Lake, Wash.—p. 669.
Challenge of Social Neuroses. W. Eliasberg, New York.—p. 676.
Pneumographic Patterns During Convulsive Therapy of Schizophrenia. E. Friedman, Norwich, Conn., and H. Barry Jr., Boston.—p. 688.
Narcoleptic Cataplectic Syndrome—Excessive and Dissociated Reaction of Sleep Mechanism—and Its Accompanying Mental States. S. Brock and B. Wiesel, New York.—p. 700.
*Familial Periodic Paralysis Associated with Exophthalmic Goiter. Alice G. Hildebrand and E. J. Kepler, Rochester, Minn.—713.
Epilepsy and Suicide. C. Prudhomme, Tuskegee, Ala.—p. 722.
Hallucinosis as Clinical Entity and Its Interpretation. A. Gordon, Philadelphia.—p. 732.

Familial Periodic Paralysis.—Hildebrand and Kepler state that exophthalmic goiter has been encountered at the Mayo Clinic in 5 of 16 patients with familial periodic paralysis. Thyroidectomy resulted in the relief of both conditions in all 5 patients.

Kentucky Medical Journal, Bowling Green

39:499-538 (Dec.) 1941

Surgery of Spleen. D. P. Hall, Louisville.—p. 501.
Value of Gastric Analysis. F. M. Stites, Louisville.—p. 507.
Evolution of Walkingiron, Turnbuckle and Joint Hinge in Fractures. M. Casper, Louisville.—p. 510.
Poliomyelitis. J. O. Nall, Marion.—p. 513.
Recent Advances in Treatment of Contagious Diseases. J. W. Bruce, Louisville.—p. 518.
False Security in Artificial Pneumothorax. P. A. Turner, Louisville.—p. 521.
Temporomandibular Joint in Relation to Eye, Ear, Nose and Throat. J. K. Hutcherson, Louisville.—p. 523.
Physician's Contribution to Religion and Human Society. W. M. Griesbaum, Louisville.—p. 526.
Sequelae of Childbirth. D. M. Cox, Louisville.—p. 528.

Nebraska State Medical Journal, Lincoln

26:415-450 (Dec.) 1941

Role of the General Medical Man in Prevention of Blindness by Early Diagnosis of Glaucoma and Other Causes of Blindness. H. S. Gradle, Chicago.—p. 415
Diagnosis and Treatment of Vesicular Eruptions of Hands and Feet. S. W. Becker, Chicago.—p. 419.
Irradiation Therapy of Cancer of Breast. A. F. Tyler, Omaha.—p. 424.
Some Clinical Aspects of Leukemia. E. B. Reed, Lincoln.—p. 429.
Later Developments in Nutrition Applicable to Surgical Problems. C. W. McLaughlin Jr., Omaha.—p. 434.
Aids in Refraction. J. H. Judd, Omaha.—p. 438.

New England Journal of Medicine, Boston

225:845-888 (Nov. 27) 1941

Fatigue in Aircraft Pilots. R. A. McFarland, Boston.—p. 845.
*Treatment of War Wounds of Brain. G. Horrax, Boston.—p. 855.
War Neuroses. D. A. Thom, Boston.—p. 864.
Blood and Blood Substitutes in Treatment of Hemorrhage, Secondary Shock and Burns. S. Mudd and E. W. Flosdorf, Philadelphia.—p. 868.
Isoimmunization in Relation to Intragroup Hemolytic Transfusion Reactions. S. B. Hooker, Boston.—p. 871.

Treatment of Cerebral War Wounds.—Horrax believes that some infections of head wounds would be prevented and some minimized if all active soldiers would have their hair cropped closely. Two other prophylactic measures are immediate administration of tetanus toxoid to all patients with compound injuries and early oral medication with a derivative of sulfanilamide. As far as surgical shock will permit, operative treatment, when indicated, should be undertaken within twelve hours of injury or earlier if possible. Other wounds of the body should also receive immediate treatment. The preoperative preparation of the patient with a wound of the head consists of stereoscopy of the head in the lateral, anteroposterior and posteroanterior positions. The whole head should then be shaved and examined for wounds of the skull. A brief neurologic examination is indicated. Not more than ⅛ to ⅙ grain (0.008 to 0.01 Gm.) of morphine may be given half an hour before operation and then only if the patient is conscious. Local anesthesia is usually indicated for gunshot wounds of the skull and of the brain. If the initial preoperative dose of morphine has not quieted the patient a second dose may be given during the operation. When local anesthesia cannot be used, anesthesia with ether or with a combination of avertin with amylene hydrate and ether is probably best. The operative treatment for all compound injuries is thorough and careful débridement of all contaminated tissues and removal, whenever possible, of foreign bodies and retained fragments of bone without adding damage to the surrounding areas. If the patient can be observed by the operator for ten days to two weeks and the operation is performed within twelve hours of injury the wound should be closed without drainage. With the oral or intravenous use of sulfanilamide derivatives and the local instillation of sulfanilamide or sulfathiazole powder many more wounds can be closed completely than was possible before the advent of chemotherapy. After operation tetanus antitoxin should be given intramuscularly, and the administration of gas gangrene antiserum is also advisable. If signs of contusion under the fractured area are evident an area of bone should be removed and the dura inspected. If the dura is tense and darkly discolored there is probably an underlying clot, and if débridement has been complete the dura should be incised, the clot evacuated and the dura resutured completely and carefully with fine silk. The author divides wounds with dural penetration caused by missiles of war into five groups and discusses the particular treatment for each: (1) the gutter type of wound, in which the missile has made a furrow through the scalp with fragments of bone, hair and clothing penetrating the underlying brain; (2) simple penetrating wounds, usually due to a large single metal fragment carrying with it fragments of bone and other débris and lodging these somewhere within the brain; (3) penetrating wounds from multiple fragments, particularly bomb splinters; (4) through and through, or perforating, injuries, usually with a small wound of entrance and a much larger wound of exit, with a certain number of fragments of bone scattered along the track, and (5) wounds involving one or another of the air sinuses, in which subsequent complications (leakage of cerebrospinal fluid or intracranial aerocele) may develop. Patients who have been

operated on should be watched carefully for ten days or longer. If infection develops the wound should be reopened and left widely open and a drain of gutta-percha or some other rubberized material should be used against the raw area of brain. When these wounds do not heal by primary union the outcome is not hopeless, as many of them finally heal with careful treatment. Frequently, even a herniation or a fungus eventually granulates and recedes and the wound epithelizes. Other acute postoperative complications are meningitis and diffuse encephalitis, and these can be treated only by keeping the pressure down by frequent lumbar punctures and by the general use of a specific derivative of sulfanilamide. Mucus in the air passages must be repeatedly cleaned out by suction to prevent atelectasis or some other pulmonary complication.

Rocky Mountain Medical Journal, Denver

38:833-936 (Nov.) 1941

Pattern for Public Education. R. L. Stearns, Boulder, Colo.—p. 850.
Relation of Problems of Industrial Medicine to Medical Preparedness. C. M. Peterson, Chicago.—p. 856.
Physician's Place in National Defense. J. F. Sharp, Salt Lake City. —p. 860.
Mycotic Infection in Northeastern Colorado: Epidermophyton of Animal Origin. A. E. Lubchenco, Sterling, Colo.—p. 862.

38:937-1024 (Dec.) 1941

Medicine Prepares. R. G. Leland, Chicago.—p. 954.
Medical Aspects of Selective Service in Colorado. P. W. Whiteley, Denver.—p. 957.
The Physician in National Defense. R. A. Bier, Washington, D. C.—p. 961.
Appreciation of the Colorado Medical Profession. R. L. Carr, Denver. —p. 969.
Cardiac Irregularities: Their Significance and Treatment. J. F. Churchill, San Diego, Calif.—p. 971.
The Acutely Ill Child: Clinical Consideration. J. M. Rector, San Francisco.—p. 978.

Southern Medical Journal, Birmingham, Ala.

34:1217-1308 (Dec.) 1941. **Partial Index**

Giants of Yesterday. P. H. Ringer, Asheville, N. C.—p. 1217.
The Sterile Couple: Analysis of Some Diagnostic and Therapeutic Data. E. C. Hamblen, Durham, N. C.—p. 1229.
Internal Podalic Version and Breech Extraction, with Comments on Recent Five Year Survey. J. W. Reddoch, New Orleans.—p. 1234.
Indication for Therapeutic Abortion in Diabetes Mellitus: Case Report. J. H. Brady, Visalia, Calif.—p. 1238.
Spontaneous Rupture of Spleen. H. Dudgeon Jr., Waco, Texas.—p. 1247.
Roentgen Management of Uterine Fibroids. E. C. Ernst, St. Louis.—p. 1249.
Subcutaneous Fibroid Syphilomas of Elbows and Knees: Report of Two Cases. L. E. Nolan and R. H. Jones, Montgomery, W. Va.—p. 1255.
Ventricular Aneurysm. D. C. Browne and G. McHardy, New Orleans. —p. 1257.
*Pustular Bacterids and Allied Conditions. G. C. Andrews, New York, and M. C. Barnes, Waco, Texas.—p. 1260.
*Vitamin K in Other Than Hemorrhagic Diseases. W. B. Rawls, New York.—p. 1266.
Observations on Health Progress of Negroes in United States During Past Two Decades. P. B. Cornely, Washington, D. C.—p. 1283.
Boric Acid Poisoning: Case Report. H. A. Peyton, Jacksonville, Fla., and D. Green, Memphis, Tenn.—p. 1286.
Potassium Permanganate Poisoning: Report of Thirty-One Cases. D. Green and O. S. Warr, Memphis, Tenn.—p. 1288.

Pustular Bacterids.—Andrews and Barnes believe that pustular lesions on the palms and soles are not pustular psoriatic lesions but rather bacterids occurring in patients with psoriasis. Pustular bacterids of the hands and feet are characterized by the following features: 1. They are chronic, symmetrically located, recalcitrant vesicular and pustular eruptions. 2. The condition has a direct relationship to focal infection. Cure results when the focal infection is removed. 3. Leukocytosis is usually present. It develops especially at the time of an exacerbation. 4. Cultures of material from the lesions are often sterile. 5. Positive cutaneous reactions are obtained to staphylococcus and streptococcus extracts, but this is perhaps of slight significance. 6. Microscopic study shows pustules deep in the epidermis, without much inflammation and without much acanthosis and parakeratosis. The microscopic changes resemble those of trichophytids.

Vitamin K for Nonhemorrhagic Diseases.—Rawls determined the prothrombin level in twenty-six nonhemorrhagic diseases and studied the effect of vitamin K on the prothrombin level in those in which it was found to be low. In osteoarthritis the mean level was 77 per cent. Treatment with vitamin K increased the level to an average of 95 per cent. The mean prothrombin level in gouty arthritis was 65 per cent. After the administration of vitamin K the level rose to 85 per cent. In 4 patients with cirrhosis of the liver the mean prothrombin level was 37 per cent, and it returned to normal with the administration of vitamin K. In carcinoma of the liver the mean prothrombin level was 48 per cent and the increase following vitamin K therapy seemed to vary with the stage of the disease and the amount of hepatic damage present. The author's observations on obstructive jaundice agree with those of other investigators that the low level can be decidedly increased by the administration of vitamin K and bile salts. The mean prothrombin level in chronic intestinal diseases (mucous colitis, ulcerative colitis, amebic dysentery with secondary anemia, chronic intestinal obstruction and chronic diarrhea) was 62 per cent, and with the administration of vitamin K it was increased to 90 per cent. The prothrombin level was also low in myelogenous leukemia, aplastic anemia, thrombocytopenia, hyperthyroidism, avitaminosis B, toxicity from gold salts and malignant endocarditis.

Southern Surgeon, Atlanta, Ga.

10:849-918 (Dec.) 1941

Free Full Thickness Skin Graft for Relief of Burn Contracture of Neck. T. G. Blocker Jr., Galveston, Texas.—p. 849.
Ruptured, Gangrenous Left Sided Appendicitis: Report of Case. W. C. Kennedy, Florence, Ala.—p. 858.
Congenital Hydrocephalus Complicating Labor: Report of Cases. E. M. Wilder and L. F. Moldavsky, Baltimore.—p. 861.
Exteriorization of Colonic Cancers. C. Rosser, Dallas, Texas.—p. 874.
Secondary Intrarectal Solid Teratoma of Ovary. M. H. Pulskamp, R. A. Griswold and F. L. Blair, Louisville, Ky.—p. 880.
Hemangioma of Terminal Ileum with Recurrent Hemorrhages from Rectum. R. J. White, Fort Worth, Texas.—p. 886.
Liposarcoma of Stomach: Report of Case. M. J. Abrams, Brewton, Ala., and J. S. Tuberville, Century, Fla.—p. 891.

Tennessee State Medical Assn. Journal, Nashville

34:423-462 (Nov.) 1941

Aviation Medicine and New Stresses in Flying. J. C. Adams, Washington, D. C.—p. 423.
Classification of Pneumonias. T. Mitchell, Memphis.—p. 434.
Specific Treatment of Pneumonia. O. N. Bryan, Nashville.—p. 437.
Nonspecific Treatment of Pneumonia. E. R. Zemp, Knoxville.—p. 439.
Prognostic Index in Pneumonia. R. P. McCombs, Philadelphia.—p. 443.

West Virginia Medical Journal, Charleston

37:529-576 (Dec.) 1941

Treatment and Healing of Operative Wounds. H. A. Bailey, in collaboration with J. C. Condry, Charleston.—p. 529.
Some Rhinologic Aspects of Chronic Bronchial Asthma. R. W. Chambers, Beckley.—p. 542.
Postpartum Care of Cervix. C. Goodhand, Parkersburg.—p. 547.
Role of Chemotherapy in Prevention and Control of Spreading Infections. I. S. Ravdin, Philadelphia.—p. 549.
Instructions To Be Given the Sterile Couple. A. P. Hudgins, Charleston.—p. 556.

Yale Journal of Biology and Medicine, New Haven

14:121-228 (Dec.) 1941

Origin of Cancer in Man in Light of Experimental Cancer Research. W. Cramer, St. Louis.—p. 121.
Effect of Local Application of Sulfonamides on Cerebral Tissue. M. Taffel and W. J. German, New Haven, Conn.—p. 139.
Observations on Response in Vitro of Pneumococcus, Staphylococcus, Alpha Hemolytic Streptococcus and Friedländer's Bacillus to Sulfonamide Drugs. J. B. Tredway and J. F. Sadusk Jr., New Haven, Conn. —p. 143.
Effect of Surface Tension Depressants on Certain Serologic Systems. Lida F. Holmes, Iowa City.—p. 155.
Effect of Combining Bacterial Toxins and X-Ray Irradiation in Treatment of Transplantable Mouse Carcinoma. E. A. Lawrence and F. Duran-Reynals, New Haven, Conn.—p. 177.
Meat Extractives and Nonprotein Nitrogen of Blood. E. Mylon and M. C. Winternitz, New Haven, Conn.—p. 183.
Anesthesia and the Electromotive Force of Nervous System. P. J. Harman, Washington, D. C.—p. 189.
Effect of Nonsuckling and Nonremoval of Milk on Individual Mammary Glands in Lactating Mouse. W. L. Williams, Rochester, N. Y. —p. 201.
Weight of Normal Heart in Adult Males. P. D. Rosahn, New Haven, Conn.—p. 209.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Archives of Disease in Childhood, London

16:147-210 (Sept.) 1941

Calory Requirements of Full Term and Premature Infants in Neonatal Period: Formula, Its Uses and Limitations. Helen M. M. Mackay. —p. 166.

*Comparison of Value of Crystalloid Solutions, Whole Blood and Blood Plasma in Treatment of Dehydration in Infancy. A. G. V. Aldridge. —p. 182.

Treatment of Dehydration in Infancy.—Aldridge states that physiologic solution of sodium chloride should not be used routinely in the treatment of dehydration brought on by gastroenteritis, for in many infants there is an apparent, if not an actual, accumulation of chloride in the blood which may increase on further administration of chloride. The routine use of whole blood is also not recommended as usually the blood, which is already concentrated, becomes even more so after transfusion. When blood transfusion is considered the hematocrit reading, and preferably the erythrocyte count and the hemoglobin concentration, should be estimated. If these are above normal transfusion is not desirable. For infants with a decided hemoconcentration who require more drastic measures than the parenteral administration of crystalloid solution the transfusion of plasma is recommended.

British Journal of Dermatology and Syphilis, London

53:299-332 (Nov.) 1941

Pyodermite Végétante (Hallopeau): Case. W. N. Goldsmith.—p. 299.
Influence of Time, Place and Contemporary History on Dermatologic Practice. T. Davies.—p. 319.

British Journal of Radiology, London

14:343-376 (Nov.) 1941

Dosage Control of Interstitial Radium Treatments by Direct Measurement of Skin Dosage Rate. W. G. Evans and H. D. Griffith.—p. 345.
Congenital Duodenal Obstruction. R. A. K. Harper.—p. 360.
Unusual Sequela to Gastroscopy. J. D. White.—p. 364.
Simple Device for Intracavitory "Contact" Therapy. T. A. Watson. —p. 366.
Mucous and Salivary Gland Tumors: Report on Series of Fifty-Seven Cases, with Special Reference to Radium Treatment. M. Lederman. —p. 368.

British Medical Journal, London

2:641-680 (Nov. 8) 1941

*Preparation and Use of Concentrated Red Cell Suspensions in Treatment of Anemia. G. E. O. Williams and T. B. Davie.—p. 641.
Mycosis Fungoides Treated by Malaria, Terminating in Hodgkin's Disease. H. MacCormac.—p. 645.
*Trinitrotoluene Health Hazard. H. M. Roberts.—p. 647.
Problem of Operation for Retroverted Uterus. Coralie Rendle-Short. —p. 649.
Simple Operation for Reduction of Fractures of Os Calcis. W. G. Campbell.—p. 651.
*Effects of Evacuation and Air Raids on City Children. W. Mary Burbury.—p. 660.

Erythrocyte Suspensions in Anemia.—Williams and Davie have given 35 patients with anemia transfusions of concentrated suspensions of erythrocytes separated from plasma. Large scale preparation of plasma from stored blood makes available considerable quantities of erythrocytes in concentrated form. In view of their potential value in the treatment of anemia it is regrettable that the cells are usually discarded. For the preparation of concentrated suspensions of erythrocytes, the aspirating needle, after the plasma is aspirated, is plunged to the bottom of the layer of erythrocytes and aspiration of the cells is continued into a fresh sterile bottle. The layer of gelatinous material on the surface of the erythrocytes is left in the bottle. The drops of cells remaining in the needle and tubing are used for grouping and cross matching. The erythrocytes of another bottle of blood of the same group, and, if necessary, of a third bottle, are added to those of the first. The concentrated suspensions are usually prepared at the request of the clinician, but at times it may be convenient to anticipate the demand by preparing a small stock of the different groups of cells. This can be stored in the refrigerator for forty-eight hours, after which time if it is not used it should be discarded. When concentrated suspensions of erythrocytes are to be given in any quantity the flow should be regulated to approximately 100 cc. an hour to avoid cardiac embarrassment. The suspensions should be used only for patients with chronic anemia who require a rapid replacement of hemoglobin and erythrocytes with a minimal increase of the circulating blood volume. Irrespective of the nature of the condition causing the anemia, transfusion of one bottle of 500 cc. of the concentrated suspension generally raises the hemoglobin between 10 and 12 per cent. The reactions following seventy-seven transfusions were considerably less than that expected to occur when stored whole blood is used.

Health Hazard of Trinitrotoluene.—Roberts points out that workers with trinitrotoluene may be affected by (1) the inhalation of the fumes of molten trinitrotoluene, (2) the inhalation of its dust into the nose, mouth and throat, with subsequent ingestion and (3) the cutaneous absorption from contact with trinitrotoluene in any of the forms mentioned. The schedule for the control of the hazard includes (1) selection of workers, (2) recording of their physical condition on entry, (3) recording of absences due to sickness, (4) periodic examinations for signs of trinitrotoluene absorption, (5) keeping a record of trinitrotoluene stains on hands, feet, underclothing (shirts and stockings) and overalls, (6) cooperation with the works chemist in carrying out the Webster test, (7) an arrangement that foremen, chargemen, supervisors or other responsible persons draw attention to workers looking piqued and to those complaining of fatigue or breathlessness, (8) insistence on protective clothing, control of dust by adequate ventilation and the washing of the hands before all meals and of the hands and the face before going home and (9) alternative work for workers who may be affected or are affected and will not admit it. Physicians in munitions areas must not believe that contact with trinitrotoluene always creates sickness. In a large munitions works manufacturing trinitrotoluene for sixteen years there has not been a single instance of serious illness, and many of the workers have been on the job all the time.

Effects of Evacuation and Air Raids on Children.—Burbury observed the effects of evacuation (and subsequent return to their homes) and of air raids on 131 children. The request for aid in some instances came because of the onset or intensification of some disorder since the war had begun. It came from a billet to which the child was evacuated, from the child or from the parents. Study revealed that some children had had behavior disorders before the war, that others came from unhappy homes and that others were lonesome away from home. Regarding the complaints, whatever the outcome, the immediate effect of evacuation (separation from parents and a known and accepted environment) is worse than the immediate effect of raiding; the waking or dream fantasy of the raid is provocative of a greater anxiety than the reality. Children were more anxious and disturbed by talk of raiding or the sound of sirens than by the raids themselves.

Irish Journal of Medical Science, Dublin

No. **189**:509-540 (Sept.) 1941

Prothrombin: Its Estimation, Clinical Significance and Treatment of Hypoprothrombinemia. M. Toohey.—p. 509.
Case of Chorionepithelioma Complicated by Staphylococcic Septicemia Successfully Treated with Sulfathiazole. E. Solomons and D. Mitchell. —p. 533.

No. **190**:541-572 (Oct.) 1941

Dextrocardia (Situs Inversus Viscerum) with Atrial Septal Defect. P. T. O'Farrell.—p. 541.
Left Heart Failure. J. Lewis.—p. 548.
Urinary Excretion of Sulfapyridine. A. E. A. Werner.—p. 558.
Hysterical Edema. M. J. Mullen and E. L. Murphy.—p. 561.

Practitioner, London

147:673-736 (Nov.) 1941

Obstetrics. J. Wyatt.—p. 673.
Anesthesia and Analgesia. C. L. Hewer.—p. 676.
Diseases of Respiratory System. W. D. W. Brooks.—p. 683.
Diseases of Kidney. R. Platt.—p. 691.
Diseases of Skin. J. T. Ingram.—p. 697.
Diseases of Eye. Ida Mann.—p. 703.
Diseases of Ear, Nose and Throat. J. H. Otty.—p. 708.
Vincent's Infection of Mouth. C. E. Kellett.—p. 714.
Coronary Thrombosis: Autopathography. H. W. Bayly.—p. 718.
Minor Surgery: V. Minor Surgery of Mouth. R. L. Newell.—p. 722.

Ophthalmologica, Basel

102:65-128 (Aug.) 1941

Etiology of Uveoparotid Fever (Heerfordt's Syndrome, Besnier-Boeck-Schaumann Disease). M. Appelmans and A. Van Horenbeeck.—p. 65.
Tumor of Optic Nerve and Its Leptomeninges in Recklinghausen's Disease. H. Goldmann and E. Grünthal.—p. 79.
*Causes of Senile Cataract: Review of Present Status of Science. J. de Ruyter.—p. 93.

102:129-192 (Sept.) 1941

Rhabdomyosarcoma of Orbit. J. François.—p. 129.
Changes of Cornea and of Conjunctiva in Boeck's Disease. C. Haldimann.—p. 138.
*Causes of Senile Cataract. J. de Ruyter.—p. 146.
Action of Low Pressure on Eye. H. F. W. Dubois and F. P. Fischer.—p. 164.

Causes of Senile Cataract.—De Ruyter summarizes the causes of senile cataract and the results of physical, chemical and clinical investigations. He raises the question as to what causes death of the cells in the lenticular fibers. Increased knowledge of life processes of the lens indicate that the causes are many. Senile cataract, the gradual decay of the cortical lenticular fibers which leaves a cell corpse behind, cannot be considered a disease entity. Death of the lenticular fibers can be caused by the aging process, by changed permeability and changed function of the lenticular epithelium or capsule (as elements of the lens fiber-aqueous humor barrier) and by defects in the blood vessels of the corpus ciliare, in the secretory function or in other elements of the blood-aqueous humor barrier. Electromagnetic oscillations may cause cataract. Defects which impair the composition of the blood, such as disturbances in the intestinal absorption of vitamins, disorders of the secretory glands (liver, thyroid, pancreas) and impairment of the regulatory mechanism for many blood constituents may also be causal factors. There exist factors in aged persons which inhibit the carbohydrate intake of the lens: 1. The dextrose content of the aqueous humor is reduced. 2. The absorption of dextrose from the aqueous humor is impaired. 3. Hexose is not readily converted into hexose-diphosphoric acid and thus cannot be reached by decomposition ferments. 4. The permeability of the lenticular capsule is reduced. Thus the lenticular capsule is inadequately supplied with carbohydrates, a factor which may readily lead to cataract. Clinical manifestations of cataract have thrown little light on possible causes. Detection of metabolic defects which may cause cataract is difficult, because they may act only intermittently. It has been definitely established that hereditary predisposition plays a part in the pathogenesis. Rational treatment of a cataract is impossible as long as its cause is not understood, and for this reason the author stresses the necessity of classifying cases of senile cataract on an etiologic basis.

Arq. do Serv. de Assist. a Psicopat. do São Paulo

6:1-242 (March-June) 1941. **Partial Index**

*Uric Acid in Cerebrospinal Fluid. J. Baptista dos Reis and A. Lara Williams.—p. 133.
Neurocanemic and Psychoanemic Syndromes. F. Tancredi.—p. 215.

Uric Acid in Cerebrospinal Fluid.—Baptista dos Reis and Lara Williams direct attention to the clinical importance of the quantitative determination of uric acid in the cerebrospinal fluid as a means of ascertaining a lowered threshold of the hematocerebrospinal barrier in the presence of an increased amount of uric acid in the blood. The small amount of uric acid in the cerebrospinal fluid and the influence of the reducing substances which are used in the quantitative determination of the substance in the fluid make the procedure difficult. The authors describe a photometric method in which the quantitative determinations are made by means of a Pulfrich photometer and Benedict's method. They made quantitative determinations of uric acid in the blood and the cerebrospinal fluid of 200 patients with mental disease and in the cerebrospinal fluid of patients with nonpsychic disease. None of the patients with mental disease presented uricacidemia or retention of nitrogen substances in the blood. The authors found that the normal amount of uric acid in the cerebrospinal fluid varies from 0.1 to 0.4 mg. of the substance for each hundred cubic centimeters of fluid. The normal ratio of uric acid in the blood and the cerebrospinal fluid is 15:1. The amount of uric acid in cerebrospinal fluid obtained by lumbar puncture is twice that which is contained in cerebrospinal fluid obtained by cisternal puncture. The amount of uric acid in the cerebrospinal fluid is increased in meningitis, cerebral hemorrhage, neurosyphilis and diabetes.

Bulletin of the Naval Medical Association, Tokyo

30:483-558 (Aug.) 1941. **Partial Index**

*Colon Bacillus Osteomyelitis. T. Muto.—p. 516.

Colon Bacillus Osteomyelitis.—Muto reports a case of chronic osteomyelitis caused by the colon bacillus in a man aged 54 who at the age of 14 had been operated on for a similar illness. The patient had recovered from the operation, but at the age of 50 the condition recurred and similar surgical treatment was instituted. This time the wound failed to heal completely and left a fistula. Still later the operative treatment was twice repeated and the patient was discharged with only a narrow fistula. Cultures of the material obtained at operation repeatedly revealed moist, semitranslucent round colonies with smooth margins, negative to Gram stain. Bacteriologic studies identified the organism as Escherichia coli communior, and the osteomyelitis was thought to be hematogenous, although several cultures of the patient's blood and excreta, as well as the contents of the gallbladder and the duodenum, gave only negative results. Suppurative osteomyelitis caused by colon bacilli is relatively rare, the literature containing records of only 7 cases. The condition presents no special clinical or pathologic picture to differentiate it from osteomyelitis due to other pyogenic organisms.

Okayama-Igakkai-Zasshi, Okayama

53:1331-1526 (July) 1941. **Partial Index**

*Serologic Studies on the Anti-Thrombocytic Serum: I. Agglutination Reaction of the Anti-Thrombocytic Serum: II. Effect of the Anti-Thrombocytic Serum on Plasma Coagulation: III. Effects of Anti-Erythrocyte and Anti-Visceral Immune Serums on Thrombocytes, Blood and Plasma Coagulation. K. Shimizu.—pp. 1438, 1453 and 1466.

Anti-Thrombocytic Serum.—Shimizu reports his investigations on the nature of guinea pig serum immunized against rabbit thrombocytes. Immune serum of high titer can be obtained after four to five injections of a 2 per cent suspension of rabbit platelets at two to six day intervals. The agglutination titer of such serum, however, diminishes rapidly, until within thirty days the immune property has completely disappeared. When the anti-thrombocyte serum is injected into rabbits the circulating platelets of the inoculated animal tend to decrease at the end of the first hour but gradually return to the normal level; corresponding changes take place in the coagulation time of the plasma. When normal serum is injected, no such noticeable fluctuation of the platelets occurs and no influence whatever can be detected on the coagulation time of the plasma. The effect of anti-thrombocytic serum in rabbits closely resembles that produced by injection of soluble toxin of nonvirulent colon bacilli. As judged from the agglutination reactions, the relationship between the platelets and erythrocytes appears to be more intimate than that between platelets and leukocytes. Injections of anti-platelet and anti-leukocyte serums in rabbits cause an almost immediate drop in circulating platelets and white blood cells, after which both these elements promptly return to their normal values; but such fluctuations in the erythrocytes are somewhat slower paced. When anti-erythrocyte serum is injected the blood platelets diminish in number, while the leukocytes tend to increase; naturally the coagulation time of the plasma appears to be definitely influenced by the quantitative changes in platelets. Injection of anti-bone marrow serum in rabbits produces a considerable reduction in the circulating platelets, while only a slight diminution occurs with administration of anti-spleen, anti-aorta and anti-kidney serums. Only the anti-bone marrow serum agglutinates blood platelets; all other types of serum giving entirely negative results. The same phenomenon is likewise observed when these serums are tested as to their precipitin reactions against platelet solution.